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# MEDICO-CHIRURGICAL TRANSACTIONS

PUBLISHED BY

THE ROYAL  
MEDICAL AND CHIRURGICAL SOCIETY  
OF  
LONDON

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VOLUME THE EIGHTY-SIXTH

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(SECOND SERIES, VOLUME THE SIXTY-EIGHTH)



LONDON  
LONGMANS, GREEN AND CO.  
(FOR THE ROYAL MEDICAL AND CHIRURGICAL SOCIETY OF LONDON)  
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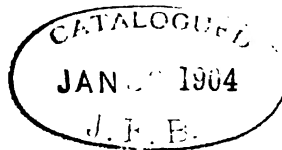
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1903



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*31st July, 1903.*



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ROYAL  
MEDICAL AND CHIRURGICAL SOCIETY  
OF LONDON

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FOR THE SESSION OF 1903-4

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# PRESIDENTS OF THE SOCIETY FROM ITS FORMATION AS THE "MEDICO-CHIRURGICAL SOCIETY," 1805

## ELECTED

- 1806 WILLIAM SAUNDERS, M.D.
- 1808 MATTHEW BAILLIE, M.D.
- 1810 SIR HENRY HALFORD, BART., M.D., G.C.H.
- 1813 SIR GILBERT BLANE, BART., M.D.
- 1816 HENRY CLINE
- 1817 WILLIAM BABINGTON, M.D.
- 1819 SIR ASTLEY PASTON COOPER, BART., K.C.H.
- 1821 JOHN COOKE, M.D.
- 1823 JOHN ABERNETHY
- 1825 GEORGE BIRKBECK, M.D.
- 1827 BENJAMIN TRAVERS
- 1829 PETER MARK ROGET, M.D.
- 1831 SIR WILLIAM LAWRENCE, BART.
- 1833 JOHN ELLIOTSON, M.D. (First President of the Society after its Incorporation as the Royal Medical and Chirurgical Society of London in 1834).
- 1835 HENRY EARLE
- 1837 RICHARD BRIGHT, M.D.
- 1839 SIR BENJAMIN COLLINS BRODIE, BART.
- 1841 ROBERT WILLIAMS, M.D.
- 1843 EDWARD STANLEY
- 1845 WILLIAM FREDERICK CHAMBERS, M.D., K.C.H.
- 1847 JAMES MONCRIEFF ARNOTT
- 1849 THOMAS ADDISON, M.D.
- 1851 JOSEPH HODGSON
- 1853 JAMES COPLAND, M.D.
- 1855 CÆSAR HENRY HAWKINS
- 1857 SIR CHARLES LOCOCK, BART., M.D.
- 1859 FREDERIC CARPENTER SKEY
- 1861 BENJAMIN GUY BABINGTON, M.D.
- 1863 RICHARD PARTRIDGE
- 1865 SIR JAMES ALDERSON, M.D.
- 1867 SAMUEL SOLLY
- 1869 SIR GEORGE BURROWS, BART., M.D.
- 1871 THOMAS BLIZARD CURLING
- 1873 CHARLES JAMES BLASIUS WILLIAMS, M.D.
- 1875 SIR JAMES PAGET, BART.
- 1877 CHARLES WEST, M.D.
- 1879 JOHN ERIC ERICHSEN
- 1881 ANDREW WHYTE BARCLAY, M.D.
- 1882 JOHN MARSHALL
- 1884 SIR GEORGE JOHNSON, M.D.
- 1886 GEORGE DAVID POLLOCK
- 1888 SIR EDWARD HENRY SIEVEKING, M.D.
- 1890 TIMOTHY HOLMES
- 1892 SIR ANDREW CLARK, BART., M.D.  
(Died 6th Nov., 1893, and Sir W. S. Church, Senior [*Medical*]  
Vice-President, acted as President until 1st March, 1894.)
- 1894 JONATHAN HUTCHINSON
- 1896 WILLIAM HOWSHIP DICKINSON, M.D.
- 1898 THOMAS BRYANT
- 1900 FREDERICK WILLIAM PAVY, M.D., LL.D., F.R.S.
- 1902 ALFRED WILLETT

## HONORARY FELLOWS

(Limited to Twelve.)

### *Elected*

- 1887 FOSTER, SIR MICHAEL, K.C.B., M.D., LL.D., F.R.S., M.P.,  
Professor of Physiology in the University of Cambridge, Nine Wells, Great Shelford, Cambridge.
- 1868 HOOKER, SIR JOSEPH DALTON, M.D., C.B., G.C.S.I., D.C.L.,  
LL.D., F.R.S., Corresponding Member of the Academy of Sciences of France; The Camp, Sunningdale.
- 1896 KELVIN, The Right Hon. LORD, P.C., G.C.V.O., F.R.S.,  
Pres. R.S.E., D.C.L., LL.D., &c., Glasgow.
- 1878 AVEBURY, The Right Hon. LORD, D.C.L., LL.D., F.R.S.,  
High Elms, Farnborough, Kent, R.S.O.
- 1887 TURNER, SIR WILLIAM, M.B., D.C.L., LL.D., F.R.S.,  
Principal of the University of Edinburgh; 6, Eton Terrace, Edinburgh.

## FOREIGN HONORARY FELLOWS

(Limited to Twenty.)

### *Elected*

- 1878 BACCELLI, GUIDO, M.D., Rome.
- 1896 VON BERGMANN, ERNST, Berlin.
- 1887 BILLINGS, JOHN S., M.D., D.C.L.Oxon., New York.
- 1896 CZERNY, VINCENT, M.D., Heidelberg.
- 1896 ERE, WILHELM, M.D., Professor of Clinical Medicine,  
Heidelberg.
- 1887 VON ESMARCH, His Excellency FRIEDRICH, M.D., Kiel.
- 1896 FOURNIER, ALFRED, M.D., Paris.
- 1896 KOCH, ROBERT, M.D., Berlin.
- 1896 KOCHER, THEODORE, M.D., Berne.
- 1868 KÖLLIKER, ALBERT, Würzburg.
- 1896 LAVERRAN, A., M.D., Paris.
- 1896 MARIE, PIERRE, M.D., Paris.
- 1896 MIRZA-ALI, M.D., Teheran.
- 1896 MITCHELL, SAMUEL WEIR, M.D., Philadelphia.

# FELLOWS

OF THE

## ROYAL MEDICAL AND CHIRURGICAL SOCIETY

### OF LONDON

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#### EXPLANATION OF THE ABBREVIATIONS

P.—President.	C.—Member of Council.
V.P.—Vice-President.	<i>Sci. Com.</i> —Member of a Scientific Committee.
T.—Treasurer.	<i>Ho. Com.</i> —Member of House Committee.
L.—Hon. Librarian.	<i>Lib. Com.</i> —Member of Library Committee.
S.—Hon. Secretary.	<i>Bldg. Com.</i> —Member of Building Committee.
	<i>Dis. Com.</i> —Member of Discussions Committee.

The abbreviations *Trans.* and *Pro.*, followed by figures, show the number of Papers which have been contributed to the *Transactions* or *Proceedings* by the Fellow whose name they follow. *Referee*, *Sci. Com.*, *Lib. Com.*, *Bldg. Com.*, *Ho. Com.*, and *Dis. Com.*, with the dates of office, are attached to the names of those who have served as Referees of papers and on the Committees of the Society.

Names printed in this *type* are of those Fellows who have paid the Composition Fee in lieu of further annual subscriptions.

Names printed in this *type* are of those Fellows who have paid the Composition Fee entitling them to receive the *Transactions*.

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#### RESIDENT FELLOWS

[N.B.—Fellows are reminded that they are, themselves, responsible for the correctness of the descriptions in the following lists, and it is particularly requested that any change of Title, Appointment, or Residence may be communicated to the Hon. Secretaries before the 1st of July in each year.]

#### *Elected*

1898 AARONS, S. JERVOIS, M.D., 14, Stratford place, Oxford street.

1877 Abercrombie, JOHN, M.D., Physician to, and Lecturer on Forensic Medicine at, Charing Cross Hospital; 23, Upper Wimpole street, Cavendish square. C. 1896-8. *Referee*, 1898—. *Trans.* 2.

*Elected*

- 1885 ABRAHAM, PHINEAS S., M.A., M.D., Dermatologist to the West London Hospital, Assistant Surgeon to Hospital for Diseases of the Skin, Blackfriars; 2, Henrietta street, Cavendish square.
- 1885 ACLAND, THEODORE DYKE, M.D., Physician to St. Thomas's Hospital, and Physician to the Hospital for Consumption and Diseases of the Chest, Brompton; 19, Bryanston square.
- 1897 ADDISON, CHRISTOPHER, M.D., Charing Cross Hospital Medical School, Chandos street.
- 1879 ALLCHIN, WILLIAM HENRY, M.D., F.R.S. Ed., Senior Physician to the Westminster Hospital; 5, Chandos street, Cavendish square. C. 1898-9. *Referee*, 1897.
- 1890 ALLINGHAM, HERBERT WILLIAM, Surgeon to His Majesty's Household; Surgeon in Ordinary to H.R.H. the Prince of Wales; Assistant Surgeon to St. George's Hospital; 25, Grosvenor street, Grosvenor square.
- 1888 ANDERSON, JOHN, M.D., C.I.E., Physician to the Seamen's Hospital, Greenwich; Lecturer on Tropical Medicine at St. Mary's Hospital Medical School; 9, Harley street, Cavendish square.
- 1891 ANDREWES, FREDERICK WILLIAM, M.D., Highwood, Hampstead lane, Highgate.
- 1902 ARMOUR, DONALD JOHN, M.B., Assistant Surgeon to the West London Hospital; Senior Assistant Surgeon to the Belgrave Hospital for Children; 89, Harley street.
- 1903 ASCHERSON, WILLIAM LAWRENCE, M.B., B.C., 37, Brunswick gardens, Camden hill.
- 1893 BAILEY, ROBERT COZENS, M.S., 21, Welbeck street, Cavendish square.
- 1891 BAKER, CHARLES ERNEST, M.B., 5, Gledhow gardens, South Kensington.
- 1900 BALDWIN, ASLETT, 6, Manchester square.
- 1887 BALL, JAMES BARRY, M.D., Physician to the West London Hospital; 12, Upper Wimpole street, Cavendish square.

***Elected***

- 1885 **BALLANCE, CHARLES ALFRED, M.S.**, Assistant Surgeon to St. Thomas's Hospital and to the Hospital for Sick Children, Great Ormond street; Surgeon to the National Hospital for the Paralysed and Epileptic, Queen square; 106, Harley street, Cavendish square. *Trans.* 6.
- 1879 **BARKER, ARTHUR EDWARD JAMES**, Professor of the Principles and Practice of Surgery and Professor of Clinical Surgery at University College, and Surgeon to University College Hospital, London; 87, Harley street, Cavendish square. C. 1895-7. *Referee*, 1897—. *Trans.* 7.
- 1876 **BARLOW, SIR THOMAS, Bart., K.C.V.O., M.D., B.S.**, *Trustee for Debenture-holders*; Physician to His Majesty's Household; Physician to University College Hospital; 10, Wimpole street, Cavendish square. C. 1892. S. 1899-1902. *Referee*, 1896-9. *Trans.* 2.
- 1902 **BAERNARD, HAROLD L., M.S.**, 21, Wimpole street.
- 1893 **BARRETT, HOWARD**, 49, Gordon square.
- 1880 **BARROW, A. BOYCE**, Surgeon to King's College Hospital; 8, Upper Wimpole street, Cavendish square. C. 1903—.
- 1896 **BARTON, JAMES KINGSTON**, 14, Ashburn place, Courtfield road, South Kensington.
- 1859 **BARWELL, RICHARD**, Consulting Surgeon to the Charing Cross Hospital; 55, Wimpole street. C. 1876-77. V.P. 1883-4. *Referee*, 1868-75, 1879-82. *Trans.* 12. *Pro.* 1.
- 1868 **BASTIAN, HENRY CHARLTON, M.A., M.D., F.R.S.**, Emeritus Professor of the Principles and Practice of Medicine and of Clinical Medicine in University College, London; Consulting Physician to University College Hospital and Physician to the National Hospital for the Paralysed and Epileptic; 8A, Manchester square. C. 1885. *Referee*, 1886-96. *Trans.* 3.

*Elected*

- 1890 BATEMAN, WILLIAM A. F., Bridge House, Richmond, Surrey.
- 1891 BATTEN, FREDERICK E., M.D., B.C., 38, Harley street.
- 1875 BEACH, FLETCHER, M.B., Physician to the West End Hospital for Nervous Diseases, Winchester House, Kingston Hill [79, Wimpole street].
- 1883 BEALE, EDWIN CLIFFORD, M.A., M.B., Physician to the City of London Hospital for Diseases of the Chest, and Physician to the Great Northern Central Hospital; 23, Upper Berkeley street.
- 1862 BEALE, LIONEL SMITH, M.B., F.R.S., Professor of the Principles and Practice of Medicine in King's College, London, and Physician to King's College Hospital; 61, Grosvenor street. C. 1876-7. *Referee*, 1873-5. *Trans.* 1.
- 1897 BEDDARD, A. P., M.D., Assistant Physician to Guy's Hospital; 44, Seymour street.
- 1880 BEEVOR, CHARLES EDWARD, M.D., Physician for Out-patients to the National Hospital for the Paralysed and Epileptic, and to the Great Northern Hospital; 135, Harley street, Cavendish square. C. 1900-2. *Referee*, 1896-1900. *Trans.* 1.
- 1901 BEEVOR, SIR HUGH REEVE, Bart., M.D., 17, Wimpole street, Cavendish square.
- 1877 BENNETT, SIR WILLIAM HENRY, K.C.V.O., Surgeon to St. George's Hospital; 1, Chesterfield street, Mayfair. C. 1893-4. *Referee*, 1892-93, 1899—. *Trans.* 4.
- 1897 BERKELEY, COMYNS, M.B., B.C., Physician to Out-Patients, Chelsea Hospital for Women; 53, Wimpole street.
- 1885 BERRY, JAMES, B.S., Surgeon to the Royal Free Hospital, and Lecturer on Surgery at the London School of Medicine for Women; Demonstrator of Practical Surgery, St. Bartholomew's Hospital; 21, Wimpole street, Cavendish square.



*Elected*

- 1893 **BIDWELL, LEONARD A.**, Senior Assistant Surgeon to the West London Hospital; 15, Upper Wimpole street, Cavendish square.
- 1851 **Birkett, JOHN, F.L.S.**, Consulting Surgeon to Guy's Hospital; Corresponding Member of the Société de Chirurgie of Paris; 1, Sussex gardens. L. 1856-7. S. 1863-5. C. 1867-8. T. 1870-78. V.P. 1879-80. *Referee*, 1851-5, 1866, 1869. *Sci. Com.* 1863. *Lib. Com.* 1852. *Trans.* 8.
- 1897 **BLACKER, G. F., M.D.**, Obstetric Physician to University College Hospital and to the Great Northern Central Hospital; 11, Wimpole street, Cavendish square.
- 1901 **BLAIKIE, J. BRUNTON, M.D., C.M.**, 22, Grosvenor street, Grosvenor square.
- 1883 **BLAND-SUTTON, JOHN**, Assistant Surgeon to the Middlesex Hospital; Surgeon to the Chelsea Hospital for Women; 47, Brook street, Grosvenor square. *Trans.* 6.
- 1865 **Blandford, GEORGE FIELDING, M.D.**, Lecturer on Psychological Medicine at St. George's Hospital; 48, Wimpole street, Cavendish square. C. 1883-4. V.P. 1898-1900.
- 1902 **BLUMFELD, JOSEPH, M.D., B.C.**, 7, Cavendish place, Cavendish square.
- 1891 **BOKENHAM, THOMAS JESSOPP**, 10, Devonshire street, Portland place.
- 1882 **Bowlby, ANTHONY ALFRED, C.M.G.**, Assistant Surgeon to St. Bartholomew's Hospital; 24, Manchester square. C. 1903—. *Trans.* 8.
- 1870 **Bowles, ROBERT LEAMON, M.D.**, 16, Upper Brook street, Grosvenor square. C. 1897-9. *Sci. Com.* 1896-1902. *Trans.* 3.
- 1886 **BOXALL, ROBERT, M.D.**, Obstetric Physician to Out-patients, and Lecturer on Midwifery and Diseases of Women, at the Middlesex Hospital; 40, Portland place.

*Elected*

- 1884 **BOYD, STANLEY, B.S.**, Surgeon to, and Lecturer on Surgery at, the Charing Cross Hospital; Surgeon to the Paddington Green Children's Hospital; Consulting Surgeon to the New Hospital for Women; 134, Harley street, Cavendish square. *Referee*, 1895—. *Trans.* 1.
- 1890 **BRADFORD, JOHN ROSE, M.D., D.Sc., F.R.S.**, Physician to University College Hospital; 8, Manchester square. *Referee*, 1899—. *Trans.* 1.
- 1897 **BRAILEY, WILLIAM ARTHUR, M.D.**, 11, Old Burlington street.
- 1901 **BREWERTON, ELMORE WRIGHT, 45, Weymouth street, Portland place.**
- 1898 **Broadbent, J. F. H., M.D.**, 35, Seymour street.
- 1868 **Broadbent, SIR WILLIAM HENRY, Bart., K.C.V.O., M.D., F.R.S., LL.D.**, Physician in Ordinary to H.M. the King; Consulting Physician to St. Mary's Hospital; Consulting Physician to the London Fever Hospital; 84, Brook street, Grosvenor square. C. 1885. *Referee*, 1881-4, 1891-7. *Trans.* 5.
- 1872 **BRODIE, GEORGE BERNARD, M.D.**, Consulting Physician-Accoucheur to Queen Charlotte's Hospital; 3, Carlos place, Grosvenor square. *Trans.* 1.
- 1880 **BROWNE, JAMES WILLIAM, M.B.**, 37, Holland Park avenue. C. 1900-1.
- 1881 **BROWNE, OSWALD AUCHINLECK, M.A., M.D.**, Physician to the Royal Hospital for Diseases of the Chest and to the Metropolitan Hospital; 7, Upper Wimpole street.
- 1874 **BRUCE, JOHN MITCHELL, M.D.**, Physician to, and Lecturer on Medicine at, the Charing Cross Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 23, Harley street. C. 1892, 1897-9. S. 1893-6. *Sci. Com.* 1889-1902. *Ho. Com.* 1898-9. *Referee*, 1886-91. *Lib. Com.* 1888-91. *Trans.* 3.
- 1898 **BRUCE, SAMUEL NOBLE, 15, Queensborough terrace, Hyde Park.**

*Elected*

- 1871 BRUNTON, SIR THOMAS LAUDER, M.D., D.Sc. LL.D., F.R.S., Physician to, and Lecturer on Pharmacology and Therapeutics at, St. Bartholomew's Hospital; 10, Stratford place, Oxford street. C. 1888-9. *Referee*, 1880-87. *Lib. Com.* 1882-7. *Trans.* 2.
- 1898 BRYANT, J. H., M.D., Assistant Physician to Guy's Hospital; 4, St. Thomas's street, London bridge.
- 1860 BRYANT, THOMAS, M.Ch., Honorary Surgeon-in-Ordinary to H.M. the King, Consulting Surgeon to Guy's Hospital; Member of the Société de Chirurgie, Paris; 27, Grosvenor street, Grosvenor square. P. 1898-1900. C. 1873-4. V.P. 1885-6. *Sci. Com.* 1863. *Referee*, 1882-4. *Lib. Com.* 1868-71. *Trans.* 17. *Pro.* 1.
- 1901 BUCKNALL, THOMAS RUPERT HAMPDEN, M.S., M.D.; 35, Harley street, Cavendish square.
- 1889 BULL, WILLIAM CHARLES, M.B., Aural Surgeon to, and Lecturer on Aural Surgery at, St. George's Hospital; 5, Clarges street, Piccadilly.
- 1893 BURGHARD, FRÉDÉRIC FRANÇOIS, M.D., M.S., Surgeon to King's College Hospital and Paddington Green Children's Hospital; 86, Harley street, Cavendish square.
- 1885 BUTLER-SMYTHE, ALBERT CHARLES, Senior Out-Patient Surgeon, Samaritan Free Hospital for Women and Children, Soho; Senior Surgeon to the Grosvenor Hospital for Women and Children; 76, Brook street, Grosvenor square.
- 1873 BUTLIN, HENRY TRENTAM, D.C.L., Surgeon to St. Bartholomew's Hospital; 82, Harley street, Cavendish square. C. 1887-8. *Referee*, 1893—. *Trans.* 4. *Pro.* 1.
- 1896 BUTTAR, CHARLES, M.D., 10, Kensington gardens square, Baywater. *Pro.* 1.

*Elected*

- 1883 BUXTON, DUDLEY WILMOT, M.D., B.S., Administrator, and Teacher of the Use, of Anæsthetics, in University College Hospital; Consulting Anæsthetist to the National Hospital for the Paralysed and Epileptic, Queen square, and Anæsthetist to the London Dental Hospital; 82, Mortimer street, Cavendish square.
- 1899 BUZZARD, EDWARD FARQUHAR, M.D., 33, Harley street Cavendish square.
- 1868 BUZZARD, THOMAS, M.D., Physician to the National Hospital for the Paralysed and Epileptic; 74, Grosvenor street, Grosvenor square. C. 1885-6. *Referee*, 1887—.
- 1885 CAHILL, JOHN, M.D., Surgeon to the Hospital of St. John and St. Elizabeth; 12, Seville street, Lowndes square.
- 1893 CALEY, HENRY ALBERT, M.D., Physician in charge of Out-patients, Lecturer on Materia Medica and Therapeutics, and Dean of the Medical School, St. Mary's Hospital; 24, Upper Berkeley street, Portman square.
- 1887 CALVERT, JAMES, M.D., 113, Harley street. *Trans.* 1.
- 1897 CANTLIE, JAMES, M.B., 46, Devonshire street.
- 1901 CARGILL, LIONEL VERNON, 31, Harley street, Cavendish square.
- 1888 CARLESS, ALBERT, M.S., Professor of Surgery in King's College, London; Surgeon to King's College Hospital; 10, Welbeck street.
- 1896 CARR, J. WALTER, M.D., Physician to the Royal Free Hospital; Physician to the Victoria Hospital for Children; 19, Cavendish place. *Trans.* 1.
- 1903 CARRUTHERS, SAMUEL WILLIAM, M.D., C.M., 44, Central hill, Norwood.
- 1898 CARTER, H. RONALD, 11, Leonard place, Kensington.
- 1853 CARTER, ROBERT BRUDENELL, Knight of Justice of the Order of St. John of Jerusalem; Consulting Ophthalmic Surgeon to St. George's Hospital; 101, Harley street, Cavendish square, and Kenilworth, Clapham common. *Trans.* 1.

*Elected*

- 1888 CAUTLEY, EDMUND, M.D., B.C., 15, Upper Brook street.  
*Trans.* 2.
- 1871 Cayley, WILLIAM, M.D., Consulting Physician to the Middlesex Hospital, Consulting Physician to the London Fever Hospital, and to the North-Eastern Hospital for Children; 27, Wimpole street, Cavendish square. C. 1888. *Referee*, 1886-7, 1899-1903. *Lib. Com.* 1886-7. *Trans.* 2.
- 1879 CHAMPNEYS, FRANCIS HENRY, M.D., Physician-Accoucheur and Lecturer on Obstetric Medicine at St. Bartholomew's Hospital; 42, Upper Brook street, Grosvenor square. C. 1898-1900. *Referee*, 1891-8. *Lib. Com.* 1885-98. *Trans.* 8.
- 1868 Cheadle, WALTER BUTLER, M.D., Physician to, and Lecturer on Clinical Medicine at, St. Mary's Hospital; Consulting Physician to the Hospital for Sick Children; 19, Portman street, Portman square. *Trustee* 1888-1903. *Marshall Hall Trustee* 1873-1903. S. 1886-8. C. 1890-91. *Sci. Com.* 1889-95. *Bldg. Com.* 1889-92. *Referee*, 1885. *Trans.* 1.
- 1879 CHEYNE, WILLIAM WATSON, C.B., M.B., F.R.S., Surgeon to King's College Hospital, and Professor of Clinical Surgery in King's College, London; 75, Harley street, Cavendish square. C. 1897-9. *Referee*, 1894-7. *Lib. Com.* 1886-8, 1891-6. *Trans.* 1.
- 1890 CHILDS, CHRISTOPHER, M.D., D.P.H., Knight of Grace of St. John, 10, Manchester square.
- 1866 Church, SIR WILLIAM SELBY, Bart., K.C.B., M.D., *Hon. Treasurer*, President of the Royal College of Physicians of London, Physician to, and Lecturer on Clinical Medicine at, St. Bartholomew's Hospital; 130, Harley street, Cavendish square. C. 1885-6. V.P. 1892-4. T. 1894—. *Referee*, 1874-81. *Ho. Com.* 1898—.
- 1879 CLARK, ANDREW, Surgeon to, and Lecturer on Surgery at, the Middlesex Hospital; 71, Harley street, Cavendish square.

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- 1882 CLARKE, ERNEST, M.D., B.S., Surgeon to the Central London Ophthalmic Hospital; Ophthalmic Surgeon to the Miller Hospital; 3, Chandos street, Cavendish square.
- 890 CLARKE, JAMES JACKSON, M.B., Assistant Surgeon to the North-West London and City Orthopædic Hospitals; 18, Portland Place.
- 1848 CLARKE, JOHN, M.D., 48, Carlisle place, Victoria street. C. 1866.
- 1888 CLARKE, ROBERT HENRY, M.B., 80, Hamlet Gardens, Ravenscourt Park.
- 1881 CLARKE, W. BRUCE, M.B., Assistant Surgeon to, and Lecturer on Anatomy at, St. Bartholomew's Hospital; Surgeon to the West London Hospital; 51, Harley street, Cavendish square. C. 1899-1901. *Trans.* 1.
- 1879 CLUTTON, HENRY HUGH, M.B., M.C., Surgeon to St. Thomas's Hospital; 2, Portland place. C. 1897-9. *Dis. Com.* 1897-8. *Referee*, 1896-7. *Trans.* 3.
- 1888 COCK, FREDERICK WILLIAM, M.D., 1, Porchester Houses Porchester square.
- 1902 COLLIER, JAMES STANSFIELD, M.D., B.Sc., 57A, Wimpole street.
- 1897 COLMAN, W. S., M.D., Assistant Physician to St. Thomas's Hospital; 9, Wimpole street.
- 1865 COOPER, SIR ALFRED, Surgeon in Ordinary to H.R.H. the Duke of Saxe-Coburg-Gotha; Consulting Surgeon to the West London Hospital and to St. Mark's Hospital; 9, Henrietta street, Cavendish square.
- 1898 CORFIELD, W. H., M.D., Professor of Hygiene and Public Health at University College, London; Medical Officer of Health for St. George's, Hanover square; 19, Savile row, and Whindown, Bexhill, Sussex.
- 1902 COTTON, HOLLAND JOHN, M.D., C.M., 33, Lowndes street.

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- 1860 **Couper, JOHN**, Consulting Surgeon to the Royal London Ophthalmic Hospital and to the London Hospital; 80, Grosvenor street. C. 1876. *Referee*, 1882-3.
- 1877 **COUPLAND, SIDNEY, M.D.**, Commissioner in Lunacy; late Physician to, and Lecturer on Medicine at, the Middlesex Hospital; 16, Queen Anne street, Cavendish square. C. 1893-4. *Referee*, 1892-3. *Ho. Com.* 1895-8.
- 1862 **Cowell, GEORGE**, Consulting Surgeon to the Westminster Hospital and to the Royal Westminster Ophthalmic Hospital; 24, Harrington gardens, South Kensington. C. 1882-3.
- 1897 **CRAWFURD, RAYMOND H. PAYNE, M.D.**, 71, Harley street.
- 1878 **CRICHTON-BROWNE, SIR JAMES, M.D., LL.D., F.R.S.**, Lord Chancellor's Visitor in Lunacy; 61, Carlisle place Mansions, Victoria street.
- 1874 **CRIPPS, WILLIAM HARRISON**, Surgeon to St. Bartholomew's Hospital; 2, Stratford place, Oxford street. C. 1890-91. *Trans.* 1.
- 1882 **CROCKER, HENRY RADCLIFFE, M.D.**, Physician to the Skin Department, University College Hospital; 121, Harley street, Cavendish square. C. 1903—. *Trans.* 3.
- 1898 **CROMBIE, ALEXANDER, C.B., M.D.**, 3, Bickenhall Mansions, Gloucester place.
- 1890 **CROWLE, THOMAS HENRY RICKARD**, 35, St. James's place.
- 1888 **CULLINGWORTH, CHARLES JAMES, M.D., D.C.L.**, Obstetric Physician and Lecturer on Diseases of Women to St. Thomas's Hospital; 14, Manchester square. *Referee*, 1896—.
- 1879 **CUMBERBATCH, A. ELKIN, M.B.**, Aural Surgeon to St. Bartholomew's Hospital, and to the National Hospital for the Paralysed and Epileptic; 80, Portland place. *Trans.* 1.

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- 1898 CURRIE, A. STARK, M.D., 81, Queen's road, Finsbury park.
- 1886 DAKIN, WILLIAM RADFORD, M.D., Obstetric Physician to, and Lecturer in Midwifery at, St. George's Hospital, and Physician to the General Lying-in Hospital; 8, Grosvenor street, Grosvenor square. *Lib. Com.* 1902—.
- 1872 DALBY, SIR WILLIAM BARTLETT, M.B., Consulting Aural Surgeon to St. George's Hospital; 18, Savile row. C. 1896-7. V.P. 1901-2. *Trans.* 4.
- 1891 DALTON, NORMAN, M.D., Physician to King's College Hospital; Professor of Pathological Anatomy in King's College, London; 4, Mansfield street, Cavendish square.
- 1896 DAUBER, JOHN HENRY, M.B., B.Ch., Assistant Physician to the Hospital for Women, Soho square; 29, Charles street, Berkeley square.
- 1889 DEAN, HENRY PERCY, M.S., Surgeon to the London Hospital; 69, Harley street, Cavendish square.
- 1878 DENT, CLINTON THOMAS, *Hon. Secretary*, Surgeon to, and Lecturer on Surgery at, St. George's Hospital; 61, Brook street. C. 1890. S. 1901—. *Bldg. Com.* 1890-2. *Referee*, 1892—1901. *Trans.* 7.
- 1891 DE SANTI, PHILIP ROBERT WILLIAM, Assistant Surgeon and Aural Surgeon to the Westminster Hospital; 15, Stratford place. *Trans.* 1.
- 1894 DICKINSON, THOMAS VINCENT, M.D., Physician to the Italian Hospital, Queen square; 33, Sloane street.
- 1859 DICKINSON, WILLIAM HOWSHIP, M.D., Consulting Physician to St. George's Hospital, and Consulting Physician to the Hospital for Sick Children; Honorary Fellow of Caius College, Cambridge; 9, Chesterfield street, Mayfair. P. 1896-8. C. 1874-5. V. P. 1887. *Referee*, 1869-73. 1882-6. *Sci. Com.* 1867, 1879, 1889-96. *Trans.* 16.



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- 1891 **DICKINSON, WILLIAM LEE, M.D.**, Assistant Physician to St. George's Hospital and to the Hospital for Sick Children; 9, Cheaterfield street, Mayfair.
- 1889 **DODD, HENRY WORK**, Surgeon to the Royal Westminster Ophthalmic Hospital; Ophthalmic Surgeon to the Royal Free Hospital and to the West-End Hospital for Nervous Diseases; 136, Harley street, Cavendish square.
- 1888 **DONELAN, JAMES, M.B., M.C.**, Physician to the Italian Hospital, Queen square; 6, Manchester square.
- 1877 **DORAN, ALBAN HENRY GRIFFITHS**, Surgeon to the Samaritan Free Hospital; 9, Granville place, Portman square. C. 1893-4. *Lib. Com.* 1891-3, 1899—. *Referee*, 1898—. *Trans.* 3.
- 1891 **DOVE, PERCY W., M.B.**, 80, Crouch hill.
- 1896 **DOWNES, JOSEPH LOCKHART, M.B., C.M.**, 269, Romford road.
- 1893 **DRYSDALE, JOHN H., M.B.**, 11, Devonshire place.
- 1865 **Duckworth, SIR DYCE, M.D., LL.D.**, Physician to, and Lecturer on Clinical Medicine at, St. Bartholomew's Hospital; 11, Grafton street, Bond street. C. 1883-4. V.P. 1902—. *Referee*, 1885-97. *Trans.* 2.
- 1880 **DUNBAR, JAMES JOHN MACWHIRTER, M.D.**, Hedingham House, Clapham Common.
- 1884 **DUNCAN, WILLIAM, M.D.**, Obstetric Physician to, and Lecturer on Midwifery at, the Middlesex Hospital; 6, Harley street, Cavendish square.
- 1887 **DUNN, HUGH PERCY**, Ophthalmic Surgeon to the West London Hospital; 54, Wimpole street, Cavendish square.
- 1898 **DUNN, L. A., M.S.**, 51, Devonshire street, Portland place.
- 1874 **DURHAM, FREDERIC, M.B.**, Senior Surgeon to the North-West London Hospital; 52, Brook street, Grosvenor square.
- 1868 **EASTES, GEORGE, M.B.** Lond. 35, Gloucester terrace, Hyde Park. C. 1892-3.

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- 1893 ECCLES, WILLIAM MCADAM, M.S., Assistant Surgeon, St. Bartholomew's Hospital, to the West London Hospital, and to the City of London Truss Society; 124, Harley street.
- 1891 EDDOWES, ALFRED, M.D., 28, Wimpole street.
- 1898 EDKINS, J. S., Brambles, Watford road, Northwood.
- 1883 EDMUNDS, WALTER, M.C., 2, Devonshire place, Portland place. *Trans.* 3.
- 1884 EDWARDS, FREDERICK SWINFORD, Surgeon to the West London Hospital, and to St. Peter's Hospital; Senior Assistant Surgeon to St. Mark's Hospital; 55, Harley street, Cavendish square.
- 1902 ENGLISH, THOMAS CRISP, 1, Park crescent, Portland place.
- 1902 EVANS, ARTHUR, M.S., 53, Queen Anne street, Cavendish square.
- 1898 EVANS, WILLMOTT H., M.D., B.S., B.Sc., Assistant Surgeon and Surgeon in charge of Skin Department, Royal Free Hospital; 2, Upper Wimpole street.
- 1879 EVE, FREDERIC S., Surgeon to the London Hospital; Surgeon to the Evelina Hospital for Sick Children; 125, Harley street, Cavendish square. C. 1897-9. *Referee*, 1902—. *Trans.* 4.
- 1877 EWART, WILLIAM, M.D., Physician to St. George's Hospital and to the Belgrave Hospital for Children; 33, Curzon street, Mayfair. C. 1895-7. *Lib. Com.* 1897—. *Sci. Com.* 1889-1902. *Trans.* 2. *Pro.* 1.
- 1900 FAIRBAIRN, JOHN SHIELDS, M.B., Assistant Obstetric Physician to St. Thomas's Hospital; 60, Wimpole street.
- 1872 FAYRE, SIR JOSEPH, Bart., K.C.S.I., LL.D., M.D., F.R.S., Surgeon-General; Physician Extraordinary to H.M. the King; late Physician to the Secretary of State for India in Council, and President of the Medical Board at the India Office; Kt. of Grace of St. John; 16 Devonshire street, Portland place. C. 1888. *Referee*, 1881-7.

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- 1898 FENWICK, E. HURRY, Surgeon to the London Hospital and to St. Peter's Hospital; 14, Savile row.
- 1880 FERRIER, DAVID, M.D., LL.D., F.R.S., Professor of Neuro-pathology in King's College, London, and Physician to King's College Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 34, Cavendish square. *Referee*, 1891-6. C. 1896-8. *Dis. Com.* 1896—. *Trans.* 2.
- 1889 FIELD, GEORGE P., Aural Surgeon to, and Lecturer on Aural Surgery at, St. Mary's Hospital; 34, Wimpole street, Cavendish square.
- 1900 FLEMMING, PERCY, M.D., B.S., Assistant Ophthalmic Surgeon to University College Hospital; Assistant Surgeon to the Royal London Ophthalmic Hospital, City road; 31, Wimpole street.
- 1891 FLETCHER, HERBERT MORLEY, M.D., Assistant Physician, East London Hospital for Children; 98, Harley street, Cavendish square.
- 1892 FORSBROOK, WILLIAM HENRY RUSSELL, M.D., 40, Lower Belgrave street, Eaton square.
- 1896 FOULERTON, ALEXANDER GRANT RUSSELL, Middlesex Hospital. *Trans.* 1.
- 1883 FOWLER, JAMES KINGSTON, M.D., Physician to, and Lecturer on Medicine at, the Middlesex Hospital; Physician to the Hospital for Consumption, Brompton, 35, Clarges street, Piccadilly. C. 1902-3. *Trans.* 1.
- 1880 FOX, THOMAS COLCOTT, B.A., M.B., Physician for Diseases of the Skin to the Westminster Hospital, and Physician to the Skin Department of the Paddington Green Hospital for Children; 14, Harley street, Cavendish square. *Trans.* 1.
- 1871 FRANK, PHILIP, M.D., 3, Elvaston place, South Kensington.

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- 1902 FRENCH, HERBERT, M.B., 26, St. Thomas's street.
- 1896 FREYER, P. J., M.D., M.Ch., Surgeon to St. Peter's Hospital; 46, Harley street, Cavendish square. *Trans.* 1.
- 1898 FRIPP, SIR ALFRED DOWNING, C.B., M.V.O., M.S., Honorary Surgeon-in-Ordinary to H.M. the King; Kt. of Grace of St. John; Assistant Surgeon to Guy's Hospital; 19, Portland place.
- 1898 FROST, WILLIAM ADAMS, Ophthalmic Surgeon to St. George's Hospital, and Surgeon to Royal Westminster Ophthalmic Hospital; 30, Cavendish square.
- 1884 FULLER, CHARLES CHINNER, 10, St. Andrew's place, Regent's Park.
- 1883 FULLER, HENRY ROXBURGH, M.D., 45, Curzon street, Mayfair.
- 1894 FURNIVALL, PERCY, Assistant Surgeon, London Hospital Assistant Surgeon, St. Mark's Hospital; 28, Weymouth street, Portland place.
- 1899 FÜRTH, KARL, M.D., 94, Harley Street.
- 1874 GALABIN, ALFRED LEWIS, M.D., Obstetric Physician to, and Lecturer on Midwifery and the Diseases of Women at, Guy's Hospital; 49, Wimpole st., Cavendish square. C. 1892. *Referee*, 1882-91, 1896—. *Lib. Com.* 1883-4. *Trans.* 2.
- 1895 GALLOWAY, JAMES, M.D., Physician, Skin Department, and Joint Lecturer on Practical Medicine, Charing Cross Hospital; 54, Harley street, Cavendish square.
- 1865 GANT, FREDERICK JAMES, Consulting Surgeon to the Royal Free Hospital; 16, Connaught square, Hyde Park. C. 1880-81. V.P. 1897-9. *Referee*, 1886-97. *Lib. Com.* 1882-5. *Trans.* 3.
- 1854 GARROD, SIR ALFRED BARING, M.D., F.R.S., Physician Extraordinary to Her late Majesty Queen Victoria; Consulting Physician to King's College Hospital; 10, Harley street, Cavendish square. C. 1867. V.P. 1880-81. *Referee*, 1855-65. *Trans.* 9.

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- 1886 GARROD, ARCHIBALD EDWARD, M.D., Assistant Physician to St. Bartholomew's Hospital; Physician to the Hospital for Sick Children, Great Ormond street; 9, Chandos street, Cavendish square. C. 1902—. *Sci. Com.* 1889-1902. *Lib. Com.* 1896-1902. *Trans.* 7.
- 1887 GAY, JOHN, 119, Upper Richmond road, Putney.
- 1866 Gee, SAMUEL JONES, M.D., *Chairman of Trustees for Debenture-holders*; Honorary Physician to H.R.H. the Prince of Wales; Physician to St. Bartholomew's Hospital; 31, Upper Brook street, Grosvenor square. C. 1883-4. L. (June) 1887-99. V.P. 1899-1900. *Sci. Com.* 1879. *Bldg. Com.* 1889-92. *Referee*, 1885-7, 1900—. *Lib. Com.* 1871-6. *Ho. Com.* 1898-1900. *Trans.* 1.
- 1898 GIBBES, CUTHBERT CHAPMAN, M.D., 89, Harley street.
- 1880 GIBBONS, ROBERT ALEXANDER, M.D., Physician to the Grosvenor Hospital for Women and Children; 29, Cadogan place. C. 1896-7. *Trans.* 1.
- 1893 GILES, ARTHUR EDWARD, M.D., B.Sc., Assistant Surgeon, Chelsea Hospital for Women; 10, Upper Wimpole street.
- 1894 GILL, RICHARD, 72, Wimpole street.
- 1877 GODLEE, RICKMAN JOHN, M.S., *Hon. Librarian*; Honorary Surgeon-in-Ordinary to H.M. the King; Surgeon to University College Hospital, and Professor of Clinical Surgery in University College, London; Surgeon to the Hospital for Consumption, Brompton; 19, Wimpole street, Cavendish square. S. 1892-4. L. 1895—. *Referee*, 1886-91. *Ho. Com.* 1898—. *Trans.* 11.
- 1870 Godson, CLEMENT, M.D., Consulting Physician to the City of London Lying-in Hospital; 82, Brook street, Grosvenor square.

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- 1886 GOLDING-BIRD, CUTHBERT HILTON, M.B., Surgeon to, and Lecturer on Clinical Surgery at, Guy's Hospital; 12, Queen Anne street, Cavendish square. *Trans.* 1.
- 1897 GOODBODY, F. W., M.D., 6, Chandos street, Cavendish square.
- 1896 GOODALL, EDWARD WILBERFORCE, M.D., B.S., Eastern Hospital, Homerton.
- 1883 GOODHART, JAMES FREDERIC, M.D., Physician to Guy's Hospital; Consulting Physician to the Evelina Hospital for Sick Children; 25, Portland place. C. 1903—. *Referee*, 1900-3. *Lib. Com.* 1893-6.
- 1889 GOODSALL, DAVID HENRY, Surgeon to the Metropolitan Hospital; Surgeon to St. Mark's Hospital; 17, Devonshire place, Upper Wimpole street.
- 1895 GOSSAGE, ALFRED MILNE, M.B., 54, Upper Berkeley street.
- 1877 GOULD, ALFRED PEARCE, M.S., Surgeon to, and Lecturer on Surgical Pathology at, the Middlesex Hospital; 10, Queen Anne street, Cavendish square. C. 1892-3. S. 1898—1901. *Referee*, 1895-8. *Ho. Com.* 1892-8. *Lib. Com.* 1891. *Trans.* 3.
- 1891 GOW, WILLIAM J., M.D., Assistant Obstetric Physician to St. Mary's Hospital; Obstetric Physician to the Royal Hospital for Women and Children; Physician to Out-Patients, Queen Charlotte's Lying-in Hospital; 27, Weymouth street, Portland place.
- 1873 GOWERS, SIR WILLIAM RICHARD, M.D., F.R.S., Consulting Physician to University College Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 50, Queen Anne street, Cavendish square. C. 1891. *Referee*, 1888-90. *Lib. Com.* 1884-6. *Trans.* 7.
- 1892 GRANT, J. DUNDAS, M.A., M.D., 18, Cavendish square.
- 1868 GREEN, T. HENRY, M.D., Physician to the Charing Cross Hospital, and to the Hospital for Consumption, Brompton; 74, Wimpole street, Cavendish square. C. 1886. *Referee*, 1882-5.

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- 1885 GRIFFITH, WALTER SPENCER ANDERSON, M.D., Assistant Physician-Accoucheur, St. Bartholomew's Hospital; Physician to Queen Charlotte's Lying-in Hospital; 96, Harley street, Cavendish square. *Referee*, 1902—.
- 1903 GRÜNBAUM, OTTO F. F., M.B., B.C., 30A, Wimpole street, Cavendish square.
- 1889 GUBB, ALFRED S., M.D., 29, Gower street.
- 1883 GUNN, ROBERT MARCUS, M.B., Surgeon to the Royal London Ophthalmic Hospital, Moorfields; Ophthalmic Surgeon to the National Hospital for the Paralysed and Epileptic; 54, Queen Anne street, Cavendish square. C. 1903—.
- 1890 GUTHRIE, LEONARD GEORGE, M.D., B.Ch., Physician to the Regent's Park Hospital for Epilepsy and Paralysis; Assistant Physician to the North-West London Hospital; Assistant Physician to the Children's Hospital, Paddington Green; 15, Upper Berkeley street, Portman square.
- 1886 HABERSHON, SAMUEL HERBERT, M.D., Assistant Physician to the Hospital for Consumption, Brompton; 88, Harley street, Cavendish square.
- 1885 HAIG, ALEXANDER, M.D., Physician to the Metropolitan Hospital, and to the Royal Hospital for Children and Women; 7, Brook street, Grosvenor square. *Trans.* 6.
- 1890 HALE, CHARLES DOUGLAS BOWDICH, M.D., 3, Sussex place, Hyde Park.
- 1881 HALL, FRANCIS DE HAVILLAND, M.D., Physician to, and Joint Lecturer on Medicine at, the Westminster Hospital; 47, Wimpole street, Cavendish square. C. 1901-3. *Referee*, 1893-7.
- 1891 HAMER, WILLIAM HEATON, M.D., 1A, Bramshill gardens Dartmouth park hill, Highgate.

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- 1889 HANDFIELD-JONES, MONTAGU, M.D., Obstetric Physician to, and Lecturer on Midwifery and Diseases of Women at, St. Mary's Hospital; Physician to the British Lying-in Hospital; 35, Cavendish square.
- 1893 HARLEY, VAUGHAN, M.D., 25, Harley street, Cavendish square.
- 1901 HARMER, WILLIAM DOUGLAS, M.B., The Warden's House, St. Bartholomew's Hospital.
- 1892 HAROLD, JOHN, M.B., 91, Harley street, Cavendish square.
- 1880 HARRIS, VINCENT DORMER, M.D., Physician to the City of London Hospital for Diseases of the Chest, Victoria Park; 22, Queen Anne street, Cavendish square. *Referee*, 1899—.
- 1870 HARRISON, REGINALD, Surgeon to St. Peter's Hospital; 6, Lower Berkeley street, Portman square. C. 1894-5. V.-P. 1898-1900. *Trans.* 4.
- 1870 HAWARD, J. WARRINGTON, *Hon. Treasurer*; Consulting Surgeon to, and Lecturer on Clinical Surgery at, St. George's Hospital; 57, Green street, Grosvenor Square. C. 1885. S. 1888-91. V.P. 1894-5. T. (June) 1895—. *Lib. Com.* 1881-4. *Sci. Com.* 1889-91. *Bldg. Com.* (Sec.) 1889-92. *Ho. Com.* 1892—. *Trans.* 3.
- 1891 HAWKINS, HERBERT PENNELL, M.D., B.Ch., Physician to St. Thomas's Hospital; 56, Portland place.
- 1875 HAYES, THOMAS CRAWFORD, M.D., Physician-Accoucheur and Physician for Diseases of Women and Children to King's College Hospital, and Professor of Midwifery in King's College; Physician for Diseases of Women to the Royal Free Hospital; 17, Clarges street, Piccadilly.
- 1891 HAYWARD, JOHN ARTHUR, M.D., 31, Lingfield road Wimbledon. *Pro.* 1.



*Elected*

- 1865 **Heath, CHRISTOPHER**, Emeritus Professor of Clinical Surgery in University College, London; and Consulting Surgeon to University College Hospital; 36, Cavendish square. C. 1880. V.P. 1889. *Lib. Com.* 1870-3. *Trans.* 4.
- 1895 **HENDERSON, EDWARD ERSKINE, B.A., M.B., B.C.**, 20, Queen Anne street, Cavendish square.
- 1901 **HENRY, JOHN PATRICK, M.D., B.Ch.**, Ophthalmic Surgeon to the Italian Hospital, Queen square; Oculist to the London School Board; 41, Welbeck street, Cavendish square.
- 1882 **HENSLEY, PHILIP JOHN, M.D.**, Physician to, and Lecturer on Forensic Medicine at, St. Bartholomew's Hospital; 4, Henrietta street, Cavendish square. *Referee*, 1897—.
- 1877 **HERMAN, GEORGE ERNEST, M.B.**, Obstetric Physician to, and Lecturer on Midwifery at, the London Hospital; 20, Harley street, Cavendish square. C. 1900-2. *Referee*, 1892-1900. *Lib. Com.* 1898-1900. *Trans.* 1.
- 1900 **HEEN, WILLIAM**, 7, Stratford place.
- 1877 **HERON, GEORGE ALLAN, M.D.**, Physician to the City of London Hospital for Diseases of the Chest, Victoria Park; 57, Harley street, Cavendish square.
- 1891 **HERRING, HERBERT T., M.B., B.S.**, 50, Harley street, Cavendish square.
- 1883 **HERRINGHAM, WILMOT PARKER, M.D.**, Assistant Physician, St. Bartholomew's Hospital; 40, Wimpole street, Cavendish square. C. 1903—. *Lib. Com.* 1902-3. *Ho. Com.* 1903—. *Trans.* 2.
- 1893 **HERSCHELL, GEORGE, M.D.**, 36, Harley street, Cavendish square.
- 1887 **HEWITT, FREDERIC WILLIAM, M.V.O., M.D.**, Honorary Anæsthetist to H.M. the King; Anæsthetist to, and Instructor in Anæsthetics at, the London Hospital; Anæsthetist at the Dental Hospital of London; 14, Queen Anne street, Cavendish square. *Trans.* 3.

*Elected*

- 1873 HIGGENS, CHARLES, Ophthalmic Surgeon to, and Lecturer on Ophthalmic Surgery at, Guy's Hospital; 52, Brook street, Grosvenor square. C. 1894-5. *Trans.* 2.
- 1890 HILL, G. WILLIAM, M.D., B.Sc., 26, Weymouth street, Portland place.
- 1899 HILLIER, ALFRED P., M.D., 30, Wimpole street.
- 1856 HOLMES, TIMOTHY, M.A., Consulting Surgeon to St. George's Hospital; Corresponding Member of the Société de Chirurgie, Paris; 6, Sussex place, Hyde Park. C. 1869-70. L. 1873-7. S. 1878-80. V.P. 1881-2. T. 1885-7. P. 1890-92. *Bldg. Com.* (*Chairman*) 1889-92. *Referee*, 1866-8, 1872, 1883-4. *Sci. Com.* 1867. *Lib. Com.* 1863-5, 1892-5. *Ho. Com.* 1892-8. *Trans.* 8.
- 1878 HOOD, DONALD WILLIAM CHARLES, C.V.O., M.D., Senior Physician to the West London Hospital; Examining Physician for King's Messengers, Foreign Office; 43, Green street, Park lane.
- 1898 HORDER, THOMAS J., M.D., 141, Harley street.
- 1883 HORSLEY, SIR VICTOR ALEXANDER HADEN, F.R.S., Surgeon to University College Hospital, Surgeon to the National Hospital for the Paralysed and Epileptic; 25, Cavendish square. *Referee*, 1897—. *Trans.* 1.
- 1896 HORTON-SMITH, PERCIVAL, M.D., 19, Devonshire street, Portland place. *Sci. Com.* 1897-1902. *Trans.* 1.
- 1892 HOWARD, R. J. BLISS, M.D., 31, Queen Anne street, Cavendish square.
- 1874 HOWSE, SIR HENRY GREENWAY, M.S., Surgeon to, and Lecturer on Surgery at, Guy's Hospital; Consulting Surgeon to the Evelina Hospital for Sick Children; 59, Brook street, Grosvenor square. C. 1890. V.P. 1899-1901. *Sci. Com.* 1879. *Referee*, 1887-9. *Trans.* 3.

*Elected*

- 1902 HULBERT, ERNEST BEDDOE, M.D., 77, Welbeck street, Cavendish square.
- 1903 HULBERT, HENRY LOUIS POWELL, St. Bartholomew's Hospital.
- 1889 HUNTER, WILLIAM, M.D., Senior Assistant Physician to the London Fever Hospital; Curator and Pathologist, Charing Cross Hospital; 103, Harley street.
- 1856 HUTCHINSON, JONATHAN, F.R.S., Consulting Surgeon to, and Emeritus Professor of Surgery at, the London Hospital; Consulting Surgeon to the Royal London Ophthalmic Hospital, Moorfields, and Senior Surgeon to the Hospital for Diseases of the Skin; 15, Cavendish square. C. 1870. V.P. 1882. P. 1894-6. *Referee*, 1876-81, 1883-94. *Lib. Com.* 1864-5. *Trans.* 15. *Pro.* 2.
- 1888 HUTCHINSON, JONATHAN, Jun., Surgeon to the London Hospital; 1, Park crescent. *Trans.* 3.
- 1897 HUTCHISON, ROBERT, M.D., 22, Queen Anne street, Cavendish square.
- 1871 JACKSON, J. HUGHLINGS, M.D., LL.D., F.R.S., Consulting Physician to the London Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 3, Manchester square. C. 1889.
- 1883 JACOBSON, WALTER HAMILTON ACLAND, M.Ch.Oxon., Assistant Surgeon to Guy's Hospital; Surgeon to the Royal Hospital for Children and Women; 66, Great Cumberland place, Hyde Park. C. 1902-3. *Referee*, 1895-1902. *Lib. Com.* 1896-1902. *Trans.* 2.
- 1897 JENNER, LOUIS, M.B., 4A, Bloomsbury square.
- 1883 JESSOP, WALTER H. H., M.B., Ophthalmic Surgeon to St. Bartholomew's Hospital; 73, Harley street. *Referee*, 1901.
- 1881 JOHNSON, GEORGE LINDSAY, M.D., Cortina, Netherhall gardens, South Hampstead, and 36, Finsbury pavement.

*Elected*

- 1889 JOHNSON, RAYMOND, M.B., B.S., Assistant Surgeon to University College Hospital; Surgeon to the Victoria Hospital for Children; 11, Wimpole street, Cavendish square. *Trans.* 1.
- 1884 JOHNSTON, JAMES, M.D., 53, Prince's square, Bayswater.
- 1899 JONES, GEORGE, M.B., 8, Church terrace, Lee.
- 1887 JONES, HENRY LEWIS, M.D., Medical Officer in charge of Electrical Department at St. Bartholomew's Hospital; 143, Harley street, Cavendish square.
- 1896 JONES, L. VERNON, B.A., M.D., B.Ch., 7, Arlington street, St. James's.
- 1881 JULER, HENRY EDWARD, Ophthalmic Surgeon to St. Mary's Hospital; Surgeon to the Royal Westminster Ophthalmic Hospital; Consulting Ophthalmic Surgeon to the London Lock Hospital; 23, Cavendish square. C. 1901-3. *Ho. Com.* 1902-3.
- 1898 KEEP, A. CORRIE, M.D., C.M., Surgeon to out-patients Samaritan Free Hospital for Women and Children; 14, Gloucester place, Portman square.
- 1882 KEETLEY, CHARLES R. B., Senior Surgeon to the West London Hospital; 56, Grosvenor street, Grosvenor square. C. 1901-3. *Lib. Com.* 1903—. *Trans.* 1.
- 1898 KELLOCK, THOMAS HERBERT, M.D., B.C., Assistant Surgeon to Middlesex Hospital and to the Hospital for Sick Children; 8, Queen Anne street, Cavendish square.
- 1901 KELYNACK, T. N., M.D., 120, Harley street.
- 1902 KERR, JAMES, M.D., D.P.H., School Board for London Victoria Embankment.
- 1857 Kiallmark, HENRY WALTER, 5, Pembridge gardens. C. 1890-91.

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- 1881 KIDD, PERCY, M.D., Physician to the Hospital for Consumption, Brompton; Physician to the London Hospital; 60, Brook street, Grosvenor square. C. 1900-2. *Trans.* 4.
- 1902 KING, DAVID BARTY, M.A., M.D., Ch.B., 18, Queen street, Mayfair.
- 1851 KINGDON, JOHN ABERNETHY, Consulting Surgeon to the Bank of England, Threadneedle street. C. 1866-7. V.P. 1872-3. *Sci. Com.* 1867. *Trans.* 1.
- 1900 LAKE, RICHARD, Surgeon Laryngologist, Mount Vernon Hospital for Consumption; Surgeon Royal Ear Hospital; 19, Harley street. *Trans.* 1.
- 1896 LANE, JAMES ERNEST, Surgeon to Out-patients, St. Mary's Hospital; 46, Queen Anne Street, Cavendish square.
- 1884 LANE, WILLIAM ARBUTHNOT, M.S., Surgeon to Guy's Hospital and to the Hospital for Sick Children, 21, Cavendish square. *Trans.* 4.
- 1882 LANG, WILLIAM, Ophthalmic Surgeon to, and Lecturer on Ophthalmic Surgery at, the Middlesex Hospital; Surgeon to the Royal London Ophthalmic Hospital, Moorfields; 22, Cavendish square.
- 1894 LANGDON-DOWN, REGINALD LANGDON, M.B., B.C., 47, Welbeck street.
- 1865 LANGTON, JOHN, Surgeon to, and Lecturer on Clinical Surgery at, St. Bartholomew's Hospital; Surgeon to the City of London Truss Society; 62, Harley street, Cavendish square. C. 1881-2. V.P. 1895-7, *Referee*, 1885-95. *Lib. Com.* 1879-80, 1888-95, *Trans.* 2.
- 1898 LATHAM, A. C., M.D., 44, Brook street, Grosvenor square.

*Elected*

- 1890 LAW, EDWARD, M.D., C.M., 8, Wimpole street, Cavendish square.
- 1898 LAWFORD, J. B., Ophthalmic Surgeon and Lecturer on Ophthalmology, St. Thomas's Hospital; Surgeon to Royal London Ophthalmic Hospital; 99, Harley street.
- 1888 LAWRENCE, LAURIE ASHER, 9, Upper Wimpole street.
- 1890 LAWRIE, EDWARD, M.B., Surgeon Lieutenant-Colonel, Indian Medical Department; late Residency Surgeon, Hyderabad, Deccan; Harley Lodge, 115A, Harley street.
- 1893 LAWSON, ARNOLD, Ophthalmic Surgeon to the Children's Hospital, Paddington Green; 12, Harley street, Cavendish square.
- 1900 LEAF, CECIL HUNTINGTON, M.A., M.B.; 75, Wimpole street, Cavendish square.
- 1896 LEE, WILLIAM EDWARD, M.D., 36, Finsbury pavement.
- 1895 LEES, DAVID BRIDGE, M.D., Physician to, and Lecturer on Medicine at, St. Mary's Hospital, and Physician to the Hospital for Sick Children; 22, Weymouth street, Portland place. *Trans.* 2.
- 1899 LEGGE, THOMAS MORISON, M.D., 2, Mitre court buildings, Temple.
- 1900 LENDON, EDWIN HARDING, M.D., 162, Holland park avenue.
- 1895 LESLIE, ROBERT MURRAY, M.B., Assistant Physician to Royal Hospital for Diseases of the Chest; 26, Harley street, Cavendish square.
- 1897 LEVY, ALFRED G., M.D., 41, Devonshire street, Portland place.
- 1886 LEWERS, ARTHUR HAMILTON NICHOLSON, M.D., Obstetric Physician to the London Hospital; 72, Harley street, Cavendish square. *Trans.* 1.

*Elected*

- 1878 LISTER, RIGHT HON. LORD, P.C., O.M., D.C.L., LL.D., F.R.S., Sergeant-Surgeon in Ordinary to H.M. the King; Emeritus Professor of Clinical Surgery in King's College, London; and Consulting Surgeon to King's College Hospital; 12, Park crescent, Regent's Park. C. 1892.
- 1891 LITTLE, ERNEST MUIRHEAD, Surgeon to the National Orthopædic Hospital; 40, Seymour street, Portman square.
- 1889 LITTLE, JOHN FLETCHER, M.B., 32, Harley street, Cavendish square.
- 1881 LOCKWOOD, CHARLES BARRETT, Surgeon to the Great Northern Central Hospital; Assistant Surgeon to, and Lecturer on Surgical and Descriptive Anatomy at, St. Bartholomew's Hospital; 19, Upper Berkeley street, Portman square. C. 1901-3. *Trans.* 5.
- 1897 LOW, HAROLD, 10, Evelyn gardens.
- 1881 LUCAS, RICHARD CLEMENT, B.S., M.B., Surgeon to, and Lecturer on Surgery, late Lecturer on Anatomy at, Guy's Hospital; Consulting Surgeon to the Evelina Hospital for Sick Children; 50, Wimpole street, Cavendish square. C. 1900-2. *Ho. Com.* 1901-2. *Trans.* 3.
- 1888 LUFF, ARTHUR PEARSON, M.D., B.Sc., Physician to Out-patients and Lecturer on Medical Jurisprudence at St. Mary's Hospital; 9, Queen Anne street, Cavendish square. *Referee*, 1903—. *Trans.* 1.
- 1887 LUSH, PERCY J. F., M.B., 4, Maresfield gardens, Hampstead.
- 1898 LYSER, C. R. C., Bolingbroke Hospital, Wandsworth common.
- 1873 MacCarthy, JEREMIAH, M.A., Consulting Surgeon to the London Hospital, late Lecturer on Surgery at the London Hospital Medical College; 1, Cambridge place, Victoria road, Kensington. C. 1886-7. *Lib. Com.* 1882-5. *Referee*, 1890—.

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- 1899 MACDONALD, GREVILLE, M.D., 85, Harley street.
- 1898 MCFADYEAN, JOHN, The Royal Veterinary College, Camden Town.
- 1894 MACFADYEN, ALLAN, M.D., C.M., Jenner Institute of Preventive Medicine, Chelsea bridge.
- 1880 MCHARDY, MALCOLM MACDONALD, Ophthalmic Surgeon to King's College Hospital, and Professor of Ophthalmic Surgery in King's College, London; Senior Surgeon to the Royal Eye Hospital, Southwark; 5, Savile row.
- 1873 MACKELLAR, ALEXANDER OBERLIN, M.Ch., Surgeon to St. Thomas's Hospital; Surgeon-in-Chief to the Metropolitan Police Force; 79, Wimpole street, Cavendish square.
- 1902 MACKENZIE, HECTOR WILLIAM GAVIN, M.A., M.D., 34, Upper Brook street.
- 1881 MACKENZIE, SIR STEPHEN, M.D., Physician to the London Hospital; Physician to the Royal London Ophthalmic Hospital; 18, Cavendish square. C. 1899-1900. *Referee*, 1890-9. *Trans.* 1.
- 1881 MACREADY, JONATHAN FORSTER CHRISTIAN HORACE, Surgeon to the Great Northern Hospital; 42, Devonshire street.
- 1880 MADDICK, EDMUND DISTIN, 31, Cavendish square.
- 1886 MAGUIRE, ROBERT, M.D., Physician to Out-patients and Joint Lecturer on Pathology at St. Mary's Hospital; Physician to the Hospital for Consumption, Brompton; 4, Seymour street, Portman square. *Sci. Com.* 1889-1902.
- 1880 MAKINS, GEORGE HENRY, C.B., Surgeon to St. Thomas's Hospital; Consulting Surgeon to the Evelina Hospital for Children; 47, Charles street, Berkeley square. C. 1899-1900. *Referee*, 1898-9, 1902—. *Trans.* 2.



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- 1885 MALCOLM, JOHN DAVID, M.B., C.M., Surgeon to the Samaritan Free Hospital; 13, Portman street, Portman square. *Trans.* 2.
- 1890 MANSON, SIR PATRICK, K.C.M.G., M.D., C.M., LL.D., F.R.S., Physician to the Seamen's Hospital, Albert Docks; Lecturer on Tropical Medicine at St. George's Hospital; 21, Queen Anne street, Cavendish square.
- 1867 MARSH, F. HOWARD, Surgeon to, and Lecturer on Surgery at, St. Bartholomew's Hospital; 30, Bruton street, Berkeley square. C. 1882-3, 1889. S. 1885-7. V.P. 1891-3. *Lib. Com.* 1880-1. *Trans.* 4.
- 1891 MARTIN, HENRY CHARRINGTON, M.D., 27, Oxford square.
- 1884 MARTIN, SIDNEY HARRIS COX, M.D., F.R.S., Assistant Physician to University College Hospital, and to the Hospital for Consumption, Brompton; Professor of Pathology, University College, London; 10, Mansfield street, Portland place.
- 1892 MASTERS, JOHN ALFRED, M.D., 31, Albert gate, Hyde Park.
- 1891 MAY, WILLIAM PAGE, M.D., B.Sc., 9, Manchester square.
- 1880 MEREDITH, WILLIAM APPLETON, M.B., C.M., Surgeon to the Samaritan Free Hospital for Women and Children; 21, Manchester square. C. 1897-9. *Ho. Com.* 1898-9. *Trans.* 1.
- 1894 MICHELS, ERNST, M.D., Surgeon to the German Hospital; 48, Finsbury square. *Trans.* 2.
- 1893 MILEY, MILES, M.B., 21, Belsize avenue, Hampstead.
- 1891 MOLINE, PAUL, M.B., 42, Walton street, Chelsea.
- 1873 MOORE, NORMAN, M.D., *Hon. Librarian*, Physician and Lecturer on Medicine to St. Bartholomew's Hospital; 94, Gloucester place, Portman square. C. 1891-2. L. 1899—. S. 1896-9. *Referee*, 1886-90. *Ho. Com.* 1898—. *Sci. Com.* 1889-1902.

*Elected*

- 1878 **MORGAN, JOHN HAMMOND, C.V.O., M.A.**, Surgeon to the Charing Cross Hospital, and to the Hospital for Sick Children, Great Ormond street; 68, Grosvenor street. C. 1895-7. *Dis. Com.* 1896-7. *Referee*, 1901—. *Trans.* 2.
- 1894 **MORISON, ALEXANDER, M.D.**, 14, Upper Berkeley street.
- 1874 **MORRIS, HENRY, M.A.**, Surgeon to the Middlesex Hospital; 8, Cavendish square. C. 1888-9. V.P. 1900-2. *Referee*, 1882-7. *Lib. Com.* 1895-6. *Trans.* 10.
- 1879 **MORRIS, MALCOLM ALEXANDER**, Surgeon to the Skin Department of, and Lecturer on Dermatology at, St. Mary's Hospital; 8, Harley street, Cavendish square. *Sci. Com.* 1889-1902. *Trans.* 1.
- 1898 **MORRISON, JAMES, M.D.**, 11, Brook street, Grosvenor square.
- 1885 **MOTT, FREDERICK WALKER, M.D., F.R.S.**, Assistant Physician, Charing Cross Hospital; Pathologist to the London County Council; 25, Nottingham place. *Referee*, 1900—. *Sci. Com.* 1899—. *Trans.* 1.
- 1902 **MUMMERY, JOHN PERCY LOCKHART, B.A.**, 10, Cavendish place.
- 1900 **MURPHY, WILLIAM REID, D.S.O.**, Lieutenant-Colonel I.M.S.; East India and Colonial Club, 16, St. James's street.
- 1896 **MURPHY, JAMES KEOGH, M.B.**, St. Bartholomew's Hospital.
- 1888 **MURRAY, HUBERT MONTAGUE, M.D.**, Physician to Out-patients, and Joint Lecturer on Medicine at, the Charing Cross Hospital; Physician to the Victoria Hospital for Children; 25, Manchester square.
- 1898 **MURRAY, JOHN**, Assistant Surgeon to the Middlesex Hospital and to the Paddington Green Children's Hospital; 110, Harley street.

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- 1880 MURRELL, WILLIAM, M.D., Physician to, Lecturer on Clinical Medicine, and Joint Lecturer on Medicine at the Westminster Hospital; 17, Welbeck street, Cavendish square. *Sci. Com.* 1889-1902. *Trans.* 1.
- 1863 MYERS, ARTHUR BOWEN RICHARDS, late Brigade-Surgeon, Brigade of Guards; 43, Gloucester street, Warwick square. C. 1878-9. *Lib. Com.* 1877.
- 1864 MUNN, THOMAS WILLIAM, Consulting Surgeon to the Middlesex Hospital; 27, York terrace, York gate.
- 1880 OGILVIE, GEORGE, M.B., B.Sc., Physician to the French Hospital, and to the Hospital for Epilepsy and Paralysis, Maida Vale; 22, Welbeck street, Cavendish square. *Trans.* 1.
- 1891 OGLE, CYRIL, M.A., M.B., Assistant Physician to St. George's Hospital; 96, Gloucester place, Portman square.
- 1858 OGLE, JOHN WILLIAM, M.D., Consulting Physician to St. George's Hospital; 96, Gloucester place, Portman square. C. 1873. V.P. 1886. *Referee*, 1864-72. *Trans.* 4.
- 1860 OGLE, WILLIAM, M.D., late Superintendent of Statistics in the Registrar-General's Department, Somerset House; 10, Gordon street, Gordon square. *Marshall Hall Trustee*, 1873-1903. S. 1868-70. C. 1876-7. V.P. 1887. *Lib. Com.* 1871-5. *Trans.* 5.
- 1892 OPENSHAW, T. HORROCKS, C.M.G., M.B., M.S., Surgeon to, and Lecturer on Anatomy at, the London Hospital; 16, Wimpole street, Cavendish square.
- 1877 ORMEROD, JOSEPH ARDERNE, M.D., Assistant Physician to St. Bartholomew's Hospital; Physician to the National Hospital for the Paralysed and Epileptic, Queen square; 25, Upper Wimpole street. C. 1897. *Lib. Com.* 1896-7. *Trans.* 1.

*Elected*

- 1879 OWEN, EDMUND, M.B., Consulting Surgeon to St. Mary's Hospital; Consulting Surgeon to the Hospital for Sick Children, Great Ormond street; Surgeon-in-chief to the French Hospital; 64, Great Cumberland place, Hyde park. C. 1896-7. *Trans.* 4.
- 1882 OWEN, SIR ISAMBAARD, M.D., Deputy-Chancellor of the University of Wales; Physician to, and Lecturer on Forensic Medicine at, St. George's Hospital; 40, Curzon street, Mayfair. C. 1902-3. *Bldg. Com.* 1889-92. *Referee*, 1893, 1895-1902.
- 1892 PAGE, H. MARMADUKE, 14, Grenville place, South Kensington.
- 1874 PAGE, HERBERT WILLIAM, M.A., M.C., Surgeon to, and Joint Lecturer on Surgery at, St. Mary's Hospital; 146, Harley street, Cavendish square. C. 1890-91. *Referee*, 1884-9. *Lib. Com.* 1886-8. *Trans.* 4.
- 1886 PAGET, STEPHEN, Surgeon to the West London Hospital; Surgeon to the Throat and Ear Department of the Middlesex Hospital; 70, Harley street. *Lib. Com.* 1902—.
- 1895 PARKER, CHARLES ARTHUR, 141, Harley street, Cavendish square.
- 1889 PARSONS, J. INGLIS, M.D., Physician to the Chelsea Hospital for Women; 3, Queen street, Mayfair.
- 1883 PASTEUR, WILLIAM, M.D., Physician to the Middlesex Hospital; Consulting Physician to the North-Eastern Hospital for Children; 4, Chandos street, Cavendish square.
- 1901 PATERSON, HERBERT JOHN, 9, Upper Wimpole street.
- 1891 PATERSON, WILLIAM BROMFIELD, 7A, Manchester square.
- 1891 PATON, EDWARD PERCY, M.D., M.S., 84, Park street, Grosvenor square.

*Elected*

- 1865 **Pavy, Frederick William, M.D., LL.D., F.R.S.**, Consulting Physician to Guy's Hospital; 35, Grosvenor street. P. 1900-2. C. 1883-4. V.P. 1893-4. *Referee*, 1871-82. *Trans.* 1.
- 1869 **PAYNE, JOSEPH FRANK, M.D.**, Physician to, and Lecturer on Medicine at, St. Thomas's Hospital; 78, Wimpole street, Cavendish square. C. 1887. *Referee*, 1890—. *Sci. Com.* 1879. *Lib. Com.* 1878-85, 1889—.
- 1894 **PEGLER, L. HEMINGTON, M.D.**, 2, Henrietta street, Cavendish square.
- 1898 **PENDLEBURY, HERBERT STRINGFELLOW, M.B., B.C.**, 44, Brook street, Grosvenor square.
- 1887 **PENROSE, FRANCIS GEORGE, M.D.**, Physician to St. George's Hospital and to the Hospital for Sick Children, Great Ormond street; 84, Wimpole street, Cavendish square. *Sci. Com.* 1889-1902.
- 1890 **PEREY, SIR EDWIN COOPER, M.D.**, Physician to, and Demonstrator of Pathology at, Guy's Hospital; The Superintendent's House, Guy's Hospital.
- 1895 **PHEAR, ARTHUR G., M.D.**, Assistant Physician and Pathologist to the Metropolitan Hospital; 47, Weymouth street, Portland place. *Trans.* 2.
- 1883 **PHILLIPS, CHARLES DOUGLAS F., M.D., LL.D.**, 10, Henrietta street, Cavendish square.
- 1884 **PHILLIPS, GEORGE RICHARD TURNER, J.P.**, 28, Palace Court, Bayswater hill.
- 1889 **PHILLIPS, SIDNEY, M.D.**, Physician and Lecturer on Medicine at St. Mary's Hospital; Senior Physician to the London Fever Hospital, and to the Lock Hospital; 62, Upper Berkeley street, Portman square. *Trans.* 1.

*Elected*

- 1867 **PICK, THOMAS PICKERING**, Consulting Surgeon to St. George's Hospital; 18, Portman street, Portman square. C. 1884-5. V.P. 1893-4. *Referee*, 1882-3, 1891-93. *Sci. Com.* 1870, 1889—. *Lib. Com.* 1879-81.
- 1884 **PITT, GEORGE NEWTON, M.D.**, *Hon. Secretary*, Physician to, and Pathologist at, Guy's Hospital; 15, Portland place. S. 1902—. *Referee*, 1897-1902. *Trans.* 1.
- 1889 **PITTS, BERNARD, M.A., M.C.**, Surgeon to St. Thomas's Hospital and Lecturer on Surgery; Surgeon to the Hospital for Sick Children, Great Ormond street; 109, Harley street, Cavendish square. *Referee*, 1897—.
- 1899 **PLAYFAIR, ERNEST, M.B.**, 57, Gloucester terrace, Hyde Park.
- 1901 **PLIMMER, HARRY GEORGE**, 16, Cheyne walk, Chelsea.
- 1885 **POLAND, JOHN**, Surgeon to the City Orthopædic Hospital and Miller Hospital, Greenwich; 2, Mansfield street, Cavendish square.
- 1884 **POLLARD, BILTON, B.S.**, Surgeon to University College Hospital; Consulting Surgeon to the North-Eastern Hospital for Children; 24, Harley street, Cavendish square. *Trans.* 1.
- 1865 **Pollock, JAMES EDWARD, M.D.**, Consulting Physician to the Hospital for Consumption, Brompton; 37, Collingham place. C. 1882-3. V.P. 1896-7. *Referee*, 1872-81.
- 1894 **POLLOCK, WILLIAM RIVERS, M.B., B.C.**, Assistant Obstetric Physician to the Westminster Hospital; 56, Park street, Grosvenor square.
- 1871 **POORE, GEORGE VIVIAN, M.D.**, Professor of Medical Jurisprudence and Clinical Medicine in University College, London; Physician to University College Hospital; 24A, Portland place. C. 1890-91. *Referee*, 1887-9, 1892—. *Lib. Com.* 1895—. *Trans.* 2.

*Elected*

- 1867 POWELL, SIR RICHARD DOUGLAS, Bart., K.C.V.O., M.D., Physician Extraordinary to H.M. the King; Physician to, and Lecturer on Medicine at, the Middlesex Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 62, Wimpole street, Cavendish square. S. (Oct.) 1883-5. C. 1887-8. V.P. 1902—. *Referee*, 1879-83, 1886. *Trans.* 3.
- 1887 POWER, D'ARCY, M.A., M.B., Assistant Surgeon at St. Bartholomew's Hospital; Surgeon to the Victoria Hospital for Children, Chelsea; 10A, Chandos street, Cavendish Square. *Lib. Com.* 1896—. *Trans.* 3.
- 1867 POWER, HENRY, Consulting Ophthalmic Surgeon to St. Bartholomew's Hospital; 10A, Chandos street, Cavendish square, and Bagdale Hall, Whitby. C. 1882-3. V.P. 1892-3. *Referee*, 1870-81, 1891-2. *Sci. Com.* 1870, 1889—. *Lib. Com.* 1872-8.
- 1883 PRINGLE, JOHN JAMES, M.B., C.M., Physician in Charge of Skin Department at the Middlesex Hospital; 23, Lower Seymour street, Portman square. *Trans.* 2.
- 1874 PURVES, WILLIAM LAIDLAW, Aural Surgeon to Guy's Hospital; 20, Stratford place, Oxford street. *Trans.* 2.
- 1877 PYE-SMITH, PHILIP HENRY, M.D., F.R.S., Physician to and Lecturer on Medicine at, Guy's Hospital; 48, Brook street, Grosvenor square. C. 1893-4. *Lib. Com.* 1887-93, 1899—. *Referee*, 1897—. *Trans.* 1.
- 1898 RAMSAY, HERBERT MURRAY, 35A, Hertford street.
- 1893 RANKIN, GUTHRIE, M.D., 4, Chesham street, Belgrave square. *Trans.* 1.
- 1899 RAWLING, LOUIS BATHE, M.B., B.C., 16, Montagu street, Portman square.
- 1892 RAYNER, HENRY, M.D., Lecturer on Psychological Medicine to St. Thomas's Hospital; 16, Queen Anne street, Cavendish square.
- 1869 READ, THOMAS LAURENCE, 11, Petersham terrace, Queen's gate. C. 1901-3. *Ho. Com.* 1902-3.

*Elected*

- 1891 REECE, RICHARD JAMES, 62, Addison gardens.
- 1882 REID, SIR JAMES, Bart., G.C.V.O., K.C.B., M.D., Physician-in-Ordinary to H.M. the King; 72, Grosvenor street, Grosvenor square.
- 1891 RENDEL, ARTHUR BOWEN, M.A., M.B., B.C., 43, Albion street, Hyde Park.
- 1887 RICHARDSON, GILBERT, M.A., M.D., 19, Putney hill.
- 1863 RINGER, SYDNEY, M.D., F.R.S., Holme Professor of Clinical Medicine in University College, London, and Physician to University College Hospital; 15, Cavendish place, Cavendish square. C. 1881-2. V.P. 1900-2. *Referee*, 1873-80, 1889-97. *Trans.* 6.
- 1900 RIVIERE, CLIVE, M.D., 19, Devonshire street, Portland place.
- 1896 ROBERTS, CHARLES HUBERT, M.D., Physician to Out-Patients, Samaritan Hospital for Women; Physician to Out-patients, Queen Charlotte's Lying-in Hospital, London; 21, Welbeck street.
- 1893 ROBERTS, D. WATKIN, M.D., 56, Manchester street, Manchester square.
- 1878 ROBERTS, FREDERICK THOMAS, M.D., Professor of Medicine, and of Clinical Medicine, in University College, London; Physician to University College Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 102, Harley street, Cavendish square. C. 1894-5. *Referee*, 1899—. *Sci. Com.* 1889-1902.
- 1898 ROBERTSON, F. W., M.D., "Ravenstone," Lingfield road, Wimbledon, Surrey.
- 1901 ROBINSON, GEORGE HENKELL DRUMMOND, M.D., 84, Park street, Grosvenor square.
- 1896 ROBINSON, HENRY BETHAM, M.S., Assistant Surgeon to, and Surgeon in Charge of the Throat Department, St. Thomas's Hospital; Assistant Surgeon to the East London Hospital for Children, Shadwell; 1, Upper Wimpole street.



*Elected*

- 1889 ROBSON, ARTHUR WILLIAM MAYO, Professor of Surgery, Yorkshire College, Leeds; Senior Surgeon, Leeds General Infirmary; 8, Park crescent, London, and 7, Park square, Leeds. *Trans.* 5. *Pro.* 1.
- 1890 ROLLESTON, HUMPHRY DAVY, M.D., Physician to, and Lecturer on Pathology at, St. George's Hospital; Senior Physician to Out-patients, Victoria Hospital for Children; 55, Upper Brook street, Grosvenor square.
- 1857 ROSE, HENRY COOPER, M.D., 16, Warwick road, Maida Vale. C. 1886-7. *Trans.* 1.
- 1888 ROUGHTON, EDMUND WILKINSON, B.S., M.D., Surgeon and Surgical Tutor to the Royal Free Hospital; 38, Queen Anne street. *Trans.* 1.
- 1882 ROUTH, AMAND JULES McCONNEL, M.D., B.S., Obstetric Physician to, and Lecturer on Midwifery at, the Charing Cross Hospital; Physician to the Samaritan Free Hospital for Women and Children; 14A, Manchester square. C. 1902—. *Lib. Com.* 1900-2. *Referee*, 1900-2.
- 1849 ROUTH, CHARLES HENRY FELIX, M.D., Consulting Physician to the Samaritan Free Hospital for Women and Children; 52, Montagu square. *Lib. Com.* 1854-5. *Trans.* 1.
- 1891 RUSSELL, J. S. RISIEN, M.D., Assistant Physician to University College Hospital, and Pathologist to the National Hospital for the Paralysed and Epileptic, Queen square; 44, Wimpole street, Cavendish square. *Trans.* 1.
- 1900 RYALL, CHARLES, 51, Queen Anne street.
- 1903 RYAN, JOHN RUSSELL, B.A., M.D., B.Ch., B.A.O., 5, Bennett street, St. James's.

*Elected*

- 1886 SAINSBURY, HARRINGTON, M.D., Physician to the Royal Free Hospital; Physician to the City of London Hospital for Diseases of the Chest; 52, Wimpole street, Cavendish square. *Trans.* 1.
- 1902 SAMBON, LOUIS W., M.D., London School of Tropical Medicine, Greenwich.
- 1899 SANDILANDS, JOHN EDWARD, M.B., 9, Sussex villas, Kensington.
- 1869 SANSOM, ARTHUR ERNEST, M.D., Physician to the London Hospital; Consulting Physician, North-Eastern Hospital for Children; 84, Harley street, Cavendish square. C. 1887-8. *Referee*, 1889—. *Trans.* 3.
- 1902 SAUNDERS, EDWARD ARTHUR, M.B., B.Ch., 49, Harley street, Cavendish square.
- 1879 SAVAGE, GEORGE HENRY, M.D., Lecturer on Mental Diseases at Guy's Hospital; 3, Henrietta street, Cavendish square. C. 1898-9.
- 1892 SCHORSTEIN, GUSTAVE M.A., M.B., B.Ch., D.P.H., Assistant Physician to the London Hospital, and to the Hospital for Consumption, Brompton; 11, Portland place.
- 1899 SCOTT, LINDLEY MARCROFT, M.D., 98, Sloane street.
- 1863 SEDGWICK, WILLIAM, 72, King Edward's gardens, Acton hill, Acton. C. 1884-5. *Trans.* 3.
- 1892 SEGUNDO, CHARLES SEMPILL DE, M.B., B.S., 6, Brook street, Hanover square.
- 1892 SELWYN-HARVEY, JOHN STEPHENSON, M.D., 1, Astwood road, Cromwell road.
- 1877 SEMON, SIR FELIX, C.V.O., M.D., Physician Extraordinary to H.M. the King; Physician for Diseases of the Throat to the National Hospital for Epilepsy and Paralysis, Queen square; 39, Wimpole street, Cavendish square. C. 1895-7. *Lib. Com.* 1894-5. *Trans.* 3.

*Elected*

- 1900 SEQUEIRA, JAMES HARRY, M.D., 13, Welbeck street.
- 1894 SEWILL, JOSEPH SEPTON, 9A, Cavendish square.
- 1882 SHARKEY, SEYMOUR JOHN, M.D., Physician to, and Joint Lecturer on Medicine at, St. Thomas's Hospital; 22, Harley street, Cavendish square. C. 1899-1900. *Referee*, 1897-9, 1902—. *Trans.* 2.
- 1900 SHAW, HAROLD BATTY, M.D., 7, Devonshire street, Portland place.
- 1886 SHAW, LAURISTON ELGIE, M.D., Physician to Guy's Hospital; 64, Harley street, Cavendish square. *Referee*, 1903—.
- 1884 SHEILD, ARTHUR MARMADUKE, M.B., B.C., Assistant Surgeon to St. George's Hospital; 4, Cavendish place. *Referee*, 1897—. *Trans.* 6.
- 1896 SHORE, THOMAS WILLIAM, M.D., Heathfield, Alleyn park, Dulwich.
- 1848 SIEVEKING, SIR EDWARD HENRY, M.D., LL.D., F.S.A., Physician Extraordinary to H.M. the King; Consulting Physician to St. Mary's and the Lock Hospitals; Kt. of Grace of St. John; 17, Manchester square. C. 1859-60. S. 1861-3. V.P. 1873-4. L. 1881-2. P. 1888-9. *Referee*, 1855-8, 1864-72, 1875-80. *Sci. Com.* 1862. *Trans.* 2.
- 1886 SILCOCK, ARTHUR QUARRY, B.S., Surgeon in charge of Outpatients, and Teacher of Operative Surgery, St. Mary's Hospital; Surgeon to the Royal London Ophthalmic Hospital; 52, Harley street, Cavendish square. *Lit. Com.* 1895—.
- 1842 SIMON, SIR JOHN, K.C.B., F.R.S., Hon. M.D. Dublin, 1887, Consulting Surgeon to St. Thomas's Hospital; 40, Kensington square. C. 1854-5. V.P. 1865. *Referee*, 1851-3, 1866-81. *Trans.* 1.
- 1899 SIMPSON, WILLIAM JOHN RITCHIE, M.D., 12, Gloucester place, Portman square.

*Elected*

- 1894 SLATER, CHARLES, M.B., 81, St. Ermin's mansions, Westminster.
- 1890 SMALE, MORTON, Surgeon Dentist to St. Mary's Hospital; 22A, Cavendish square.
- 1879 SMITH, E. NOBLE, Surgeon to the City Orthopædic Hospital; Surgeon to All Saints' Children's Hospital; Orthopædic Surgeon to the British Home for Incurables; 24, Queen Anne street, Cavendish square.
- 1881 SMITH, EUSTACE, M.D., Physician to H.M. the King of the Belgians; Physician to the East London Children's Hospital, and to the Victoria Park Hospital for Diseases of the Chest, 15, Queen Anne street, Cavendish square. C. 1899-1900.
- 1866 SMITH, HEYWOOD, M.A., M.D., 25, Welbeck street, Cavendish square. JAN 30 1904
- 1889 SMITH, ROBERT PERCY, M.D., B.S., Lecturer on Psychological Medicine, Charing Cross Hospital; 36, Queen Anne street.
- 1863 SMITH, SIR THOMAS, Bart., K.C.V.O., Honorary Sergeant-Surgeon to H.M. the King; Consulting Surgeon to St. Bartholomew's Hospital; 5, Stratford place, Oxford street. *Marshall Hall Trustee*, 1877-1903. S. 1870-2. C. 1875-6. V.P. 1887-8. *Referee*, 1873-4, 1880-6. *Sci. Com.* 1867. *Trans.* 4.
- 1872 SMITH, THOMAS GILBERT, M.D., Physician to the London Hospital; Physician to the Royal Hospital for Diseases of the Chest, City road; 68, Harley street, Cavendish square. C. 1890. *Trans.* 1.
- 1873 SMITH, W. JOHNSON, Surgeon to the Seamen's Hospital Society, Greenwich.
- 1874 SMITH, WILLIAM ROBERT, M.D., D.Sc., F.R.S. Edin., Barrister-at-Law, Professor of Forensic Medicine, and Director of the Laboratories of State Medicine in King's College, London; 74, Great Russell street. *Trans.* 1.

*Elected*

- 1889 SPENCER, HERBERT R., M.D., B.S., Professor of Midwifery in University College; Obstetric Physician to University College Hospital; 104, Harley street. *Referee*, 1894—.
- 1887 SPENCER, WALTER GEORGE, M.B., M.S., Surgeon to, and Lecturer on Physiology at, the Westminster Hospital; 35, Brook street, Grosvenor square. *Trans.* 2.
- 1888 SPICER, ROBERT HENRY SCANES, M.D., Surgeon to the Department for Diseases of the Throat, St. Mary's Hospital; 28, Welbeck street, Cavendish square.
- 1890 SPICER, WILLIAM THOMAS HOLMES, M.B., Ophthalmic Surgeon to St. Bartholomew's Hospital; Surgeon to the Royal London Ophthalmic Hospital (City road, late Moorfields); Consulting Ophthalmic Surgeon to the Metropolitan Hospital; 5, Wimpole street, Cavendish square.
- 1875 SPITTA, EDMUND JOHNSON, Ivy House, 31, South Side, Clapham Common, Surrey. C. 1903—.
- 1903 SPRIGGS, EDMUND IVENS, M.D., 26, St. Thomas's street.
- 1885 SQUIRE, JOHN EDWARD, M.D., Physician to the Mount Vernon Hospital for Consumption; 5, Harley street, Cavendish square. *Trans.* 2.
- 1897 STAINER, EDWARD, M.A., M.B., 60, Wimpole street.
- 1896 STEPHENS, JOHN WILLIAM WATSON, M.B., B.C., 8, Fopstone road, Earl's Court.
- 1899 STEWART, PURVES, M.D., 7, Harley street. *Trans.* 1.
- 1856 Stocker, ALONZO HENRY, M.D., Peckham House, Peckham.
- 1884 STONHAM, CHARLES, C.M.G., Surgeon to, and Lecturer on Surgery and Teacher of Operative Surgery at, the Westminster Hospital; Surgeon to the Poplar Hospital for Accidents; 4, Harley street, Cavendish square.

*Elected*

- 1896 SUTHERLAND, GEORGE ALEXANDER, M.D., Physician to Paddington Green Children's Hospital; Assistant Physician to the North-West London Hospital; 73, Wimpole street, Cavendish square.
- 1896 SWAN, CHARLES ROBERT JOHN ATKIN, M.B., B.Ch., 4, Devonport street, Hyde Park.
- 1890 SYERS, HENRY WALTER, M.D., 75, Wimpole street.
- 1886 SYMONDS, CHARTERS JAMES, M.S., M.D., Surgeon to, and Surgeon in charge of the Throat Department at, Guy's Hospital; 58, Portland place.
- 1903 TALBOT, EUSTACE, M.B., 10, Great George street, Westminster.
- 1875 TAY, WARREN, Senior Surgeon to the London Hospital, to the Royal London Ophthalmic Hospital, and to the Hospital for Diseases of the Skin, Blackfriars; Consulting Surgeon to the North-Eastern Hospital for Children; 4, Finsbury square.
- 1873 TAYLOR, FREDERICK, M.D., Physician to, and Lecturer on Medicine at, Guy's Hospital; Consulting Physician to the Evelina Hospital for Sick Children; 20, Wimpole street, Cavendish square. *Trustee*, 1893-1903. *S.* 1889-93. *C.* 1894-6. *Sci. Com.* 1889-1902. *Referee*, 1887-8, 1899—. *Trans.* 3.
- 1893 TAYLOR, JAMES, M.D., Assistant Physician to the National Hospital for the Paralysed and Epileptic; Physician to the North-Eastern Hospital for Children, and to the National Orthopædic Hospital; 49, Welbeck street, Cavendish square. *Trans.* 1.
- 1890 TAYLOR, SEYMOUR, M.D., Assistant Physician, West London Hospital; 16, Seymour street, Portman square.
- 1874 THIN, GEORGE, M.D., 63, Harley street, Cavendish square. *C.* 1893-4. *Trans.* 14.
- 1900 THOMPSON, CHARLES HERBERT, M.D., 133, Harley street Cavendish square.

*Elected*

- 1862 **Thompson, EDMUND SYMES, M.D.**, Consulting Physician to the Hospital for Consumption, Brompton; Gresham Professor of Medicine; 33, Cavendish square. S. 1871-4. C. 1878-9. *Sci. Com.* 1889-1902. *Referee*, 1876-7. *Trans.* 1.
- 1852 **Thompson, SIR HENRY, Bart.**, Surgeon-Extraordinary to H.M. the King of the Belgians; Emeritus Professor of Clinical Surgery in University College, London; and Consulting Surgeon to University College Hospital; 35, Wimpole street, Cavendish square. V.P. 1888. C. 1869. *Trans.* 8.
- 1862 **Thompson, REGINALD EDWARD, M.D.**, 13, Cheyne gardens, Chelsea. C. 1879. S. 1880-82. V.P. 1883-4. *Referee*, 1873-8. *Sci. Com.* 1867. *Trans.* 2.
- 1899 **Thomson, HERBERT CAMPBELL, M.D.**, 34, Queen Anne street. *Trans.* 2.
- 1892 **Thomson, StCLAIR, M.D.**, Physician to the Throat Hospital, Golden Square; Surgeon to the Royal Ear Hospital, London; 28, Queen Anne street, Cavendish square. *Trans.* 1.
- 1900 **Thomson-Walker, JOHN WILLIAM, M.B.**, 8, Cavendish place.
- 1892 **Thorne, WILLIAM BEZLY, M.D.**, 53, Upper Brook street.
- 1899 **Thursfield, JAMES HUGH, M.D.**, 45, Weymouth street, Portland place. *Trans.* 1.
- 1889 **Tirard, NESTOR ISIDORE CHARLES, M.D.**, Professor of the Principles and Practice of Medicine, King's College; Physician to King's College Hospital, and Physician to the Evelina Hospital for Sick Children; 74, Harley street, Cavendish square.
- 1872 **Tomes, CHARLES SISSMORE, M.A., F.R.S.**, 9, Park crescent, Portland place. C. 1887. V.P. 1897-99. *Lib. Com.* 1879.

*Elected*

- 1882 **TOOTH, HOWARD HENRY, C.M.G., M.D.**, Physician to the National Hospital for the Paralysed and Epileptic, Queen square; Assistant Physician to St. Bartholomew's Hospital; 34, Harley street, Cavendish square. *Referee*, 1902—. *Sci. Com.* 1896-1902.
- 1879 **Treves, SIR FREDERICK, Bart., C.B., K.C.V.O., LL.D.**, Sergeant-Surgeon in Ordinary to H.M. the King; Surgeon in Ordinary to H.R.H. the Prince of Wales; Kt. of Grace of St. John; Consulting Surgeon to the London Hospital; 6, Wimpole street, Cavendish square. *C.* 1895-6. *Referee*, 1890-95. *Sci. Com.* 1889-95. *Trans.* 6.
- 1902 **TREVOR, ROBERT SALUSBURY, M.B., B.C.**, 21, FitzGeorge avenue, West Kensington.
- 1859 **Truman, EDWIN THOMAS**, Surgeon - Dentist to His Majesty's Household; 23, Old Burlington street.
- 1897 **TUNNICLIFFE, FRANCIS WHITTAKER, M.D.**, 6, Devonshire street, Portland place.
- 1889 **TURNBULL, GEORGE LINDSAY, M.D.**, 47, Ladbroke square.
- 1882 **TURNER, GEORGE ROBERTSON**, Surgeon to, and Joint Lecturer on Surgery at, St. George's Hospital; 41, Half Moon street, Piccadilly. *C.* 1903—. *Trans.* 1.
- 1898 **TURNER, WILLIAM, M.B., B.S.**, Assistant Surgeon, Westminster Hospital; 53, Queen Anne street, Cavendish square.
- 1896 **TURNER, WILLIAM ALDREN, M.D.**, Assistant Physician to King's College Hospital and to the National Hospital for the Paralysed and Epileptic, Queen Square; 13, Queen Anne street, Cavendish square. *Trans.* 1.
- 1896 **TURNER, HORACE GEORGE, M.D.**, Joint Lecturer on Pathology and Assistant Physician to St. Thomas's Hospital; 68, Portland place. *Trans.* 1.



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- 1892 TWEEDY, JOHN, Professor of Ophthalmic Medicine and Surgery in University College, Ophthalmic Surgeon to University College Hospital, and Surgeon to the Royal London Ophthalmic Hospital; 100, Harley street, Cavendish square.
- 1876 VENN, ALBERT JOHN, M.D., 63, Grosvenor street.
- 1870 VENNING, EDGCOMBE, 30, Cadogan place. C. 1898-1900. V.P. 1902—. *Ho. Com.* 1903—.
- 1902 VINCENT, RALPH, M.D., B.S., 1, Harley street.
- 1891 VOELCKER, ARTHUR FRANCIS, M.D., B.S., Assistant Physician to, and Lecturer on Pathology at, the Middlesex Hospital; Assistant Physician, Hospital for Sick Children, Great Ormond street; 101, Harley street.
- 1896 WAGGETT, ERNEST, M.B., B.C., Surgeon, London Throat Hospital; Surgeon to Out Patient Throat and Ear Department, Great Northern Central Hospital; 45, Upper Brook street.
- 1884 WAKLEY, THOMAS, jun., 5, Queen's Gate, South Kensington.
- 1896 WALDO, FREDERICK JOSEPH, M.D., City Coroner, 40, Lansdowne road, Holland park.
- 1900 WALKER, H. ROE, 8, Harley street, Cavendish square.
- 1887 WALLACE, EDWARD JAMES, M.D., 22, Hans crescent, Chelsea.
- 1883 WALLER, AUGUSTUS, M.D., F.R.S., Lecturer on Physiology, St. Mary's Hospital; Weston Lodge, 32, Grove End road, St. John's Wood. *Referee*, 1895—.
- 1888 WALLIS, FREDERICK CHARLES, M.B., B.C., Assistant Surgeon to the Charing Cross Hospital; 107, Harley street, Cavendish square.

*Elected*

- 1896 WALSHAM, HUGH, M.A., M.D., Assistant Physician to the City of London Hospital for Diseases of the Chest; Assistant Medical Officer in Electrical Department, St. Bartholomew's Hospital; 114, Harley street, Cavendish square.
- 1873 WALSHAM, WILLIAM JOHNSON, C.M., Surgeon to, and Lecturer on Surgery at, St. Bartholomew's Hospital; Consulting Surgeon to the Metropolitan Hospital; 77, Harley Street, Cavendish square. C. 1888-9. *Referee*, 1895—. *Lib. Com.* 1882-5. *Trans.* 8.
- 1886 WARD, ALLAN OGIER, M.D., 73, Cheapside.
- 1890 WARD, ARTHUR HENRY, Surgeon to Out-patients, Lock Hospital; 31, Grosvenor street.
- 1894 WARD-HUMPHREYS, GEORGE HERBERT, 26, Charles street, St. James's.
- 1891 WARING, H. J., M.B., M.S., B.Sc., Assistant Surgeon and Demonstrator of Operative Surgery, St. Bartholomew's Hospital; Surgeon, Metropolitan Hospital; 37, Wimpole street.
- 1877 WARNER, FRANCIS, M.D., Physician to, and Lecturer on Materia Medica and Therapeutics at, the London Hospital; 5, Prince of Wales terrace, Kensington Palace. C. 1899-1901. *Trans.* 3.
- 1894 WATERHOUSE, HERBERT FURNIVALL, C.M., Senior Assistant Surgeon and Lecturer on Anatomy, Charing Cross Hospital; Surgeon, Victoria Hospital for Children; 81, Wimpole street.
- 1861 WATSON, WILLIAM SPENCER, M.B., 61, Bedford gardens, Campden hill, Kensington. C. 1883-4. *Trans.* 1.
- 1891 WEBER, FREDERIC PARKES, M.D., Physician to the German Hospital, Dalston; 19, Harley street. *Trans.* 2. *Pro.* 1.

*Elected*

- 1857 WEBER, SIR HERMANN, M.D., Consulting Physician to the German Hospital; 10, Grosvenor street, Grosvenor square. C. 1874-5. V.P. 1885-6. *Sci. Com.* 1889-1902. *Referee*, 1869-73, 1878-84. *Lib. Com.* 1864-73. *Trans.* 6.
- 1895 WELLS, SYDNEY RUSSELL, M.D., 24, Somerset street Portman square.
- 1877 WEST, SAMUEL, M.D., Assistant Physician to St. Bartholomew's Hospital; Senior Physician to the Royal Free Hospital; 15, Wimpole street, Cavendish square. C. 1894-5. *Lib. Com.* 1892-4. *Trans.* 7.
- 1888 WETHERED, FRANK JOSEPH, M.D., Assistant Physician to the Hospital for Consumption, Brompton; 83, Harley street, Cavendish square. *Trans.* 1.
- 1881 WHARRY, ROBERT, M.D., 7, Cambridge gate, Regent's park.
- 1875 WHIPHAM, THOMAS TILLYER, M.D., Consulting Physician to St. George's Hospital; 11, Grosvenor street, Grosvenor square. C. 1892-3.
- 1891 WHITE, CHARLES PERCIVAL, M.B., B.C., 22, Cadogan gardens.
- 1897 WHITE, CHARLES POWELL, Pathological Department, St. Thomas's Hospital.
- 1881 WHITE, WILLIAM HALE, M.D., Physician to, and Lecturer on Materia Medica at, Guy's Hospital; 65, Harley street, Cavendish square. C. 1900-2. *Referee*, 1888-97, 1899-1900. *Trans.* 4.
- 1890 WHITE-COOPER, W. G. O., M.B., 5, Courtfield road, Gloucester road.
- 1897 WHITFIELD, ARTHUR, M.D., 21, Bentinck street, Manchester square. *Trans.* 1.
- 1899 WHITING, ARTHUR J., M.D., 142, Harley street.
- 1902 WIGHTWICK, FALLON PERCY, M.D., 9A, Upper Brook street.

*Elected*

- 1863 **Wilks, SIR SAMUEL, Bart., M.D., LL.D., F.R.S.**, Physician Extraordinary to Her late Majesty Queen Victoria, Physician in Ordinary to their Royal Highnesses the Duke and Duchess of Connaught; Consulting Physician to Guy's Hospital; 8, Prince Arthur road, Hampstead. *Referee*, 1872-81.
- 1890 **WILLCOCKS, FREDERICK, M.D.**, Physician to Out-Patients, and Lecturer on Materia Medica and Therapeutics, at the Charing Cross Hospital; Physician to the Evelina Hospital for Sick Children; 14, Mandeville place, Manchester square.
- 1865 **Willett, ALFRED, President**; Surgeon to St. Bartholomew's Hospital; Surgeon to St. Luke's Hospital; 36, Wimpole street, Cavendish square. *Trustee*, 1892-1903. C. 1880-1. V.P. 1890-1. P. 1902—. *Referee*, 1882-9, 1892-1902. *Bldg. Com.* 1889-92. *Ho. Com.* 1892-8. *Trans.* 2.
- 1887 **WILLETT, EDGAR, M.B.**, 22, Queen Anne street, Cavendish square.
- 1902 **Willett, JOHN ABERNETHY, M.B.**, 36, Wimpole street, Cavendish square.
- 1888 **WILLIAMS, CAMPBELL, 18**, Queen Anne street.
- 1866 **Williams, CHARLES THEODORE, M.A., M.D.**, *Trustee for Debenture-holders*; Consulting Physician to the Hospital for Consumption and Diseases of the Chest, Brompton; 2, Upper Brook street, Grosvenor square. C. 1884-5. V.P. 1900-2. *Referee*, 1888-1900. *Lib. Com.* 1880-3. *Ho. Com.* 1900-2. *Sci. Com.* 1889-1902. *Trans.* 6.
- 1881 **WILLIAMS, DAWSON, M.D.**, Physician to the East London Hospital for Children; 2, Wyndham place, Bryanston square. *Trans.* 1.

*Elected*

- 1901 WILLIAMS, LEONARD, M.D., 8, York street, Portman square.
- 1903 WILLIAMSON, OLIVER K., M.A., M.D., 50, Upper Berkeley street.
- 1890 WILLS, WILLIAM ALFRED, M.D., Assistant Physician to the Westminster Hospital; Senior Physician to the North-Eastern Hospital for Children; 29, Lower Seymour street, Portman square.
- 1879 WOAKES, EDWARD, M.D., Senior Aural Surgeon to the London Hospital; 78, Harley street, Cavendish square.
- 1887 WOOD, THOMAS OUTTERSON, M.D., Senior Physician to the West End Hospital for Nervous Diseases; 40, Margaret street, Cavendish square.
- 1891 WOODFORD, ALFRED POWNALL, 160, Goldhawk road, Shepherd's Bush.
- 1892 WRIGHT, ALMROTH EDWARD, M.D., Ch.B., 7, Lower Seymour street. *Trans.* 1.
- 1890 WYNTER, WALTER ESSEX, M.D., Physician to the Middlesex Hospital; 30, Upper Berkeley street, Portman square.

# LIST OF RESIDENT FELLOWS

ARRANGED ACCORDING TO

DATE OF ELECTION

- |      |   |      |   |
|------|---|------|---|
| 1842 | Sir John Simon, K.C.B., F.R.S.  | 1863 | Sydney Ringer, M.D., F.R.S.   |
| 1848 | Sir Edward H. Sieveking, M.D.<br>John Clarke, M.D.  |      | Sir Thomas Smith, Bart., K.C.V.O.<br>Arthur B. R. Myers.<br>William Sedgwick.   |
| 1849 | C. H. F. Routh, M.D.  | 1864 | Thomas William Nunn.  |
| 1851 | John Birkett.<br>John A. Kingdon.   | 1865 | James Edward Pollock, M.D.<br>George Fielding Blandford, M.D.<br>Sir Dyce Duckworth, M.D.<br>Frederick W. Pavy, M.D., F.R.S.<br>John Langton.<br>Frederick James Gant.<br>Alfred Willett.<br>Sir Alfred Cooper.<br>Christopher Heath. |
| 1852 | Sir Henry Thompson, Bart.   | 1866 | Samuel Jones Gee, M.D.<br>Charles Theodore Williams, M.D.<br>Heywood Smith, M.D.<br>Sir William Selby Church, Bart.,<br>K.C.B., M.D.  |
| 1853 | Robert Brudenell Carter.  | 1867 | Sir R. Douglas Powell, Bart., M.D.<br>F. Howard Marsh.<br>Henry Power.<br>Thomas Pickering Pick.  |
| 1854 | Sir Alfred B. Garrod, M.D., F.R.S.  | 1868 | H. Charlton Bastian, M.D., F.R.S.<br>Sir W. H. Broadbent, Bart., M.D.,<br>K.C.V.O., F.R.S.<br>Thomas Buzzard, M.D.<br>Walter Butler Cheadle, M.D.   |
| 1856 | Jonathan Hutchinson, F.R.S.<br>Timothy Holmes.<br>Alonzo H. Stocker, M.D.   |      |   |
| 1857 | Sir Hermann Weber, M.D.<br>Henry Cooper Rose, M.D.<br>Henry Walter Kialmark.  |      |   |
| 1858 | John William Ogle, M.D.   |      |   |
| 1859 | Wm. Howship Dickinson, M.D.<br>Edwin Thomas Truman.<br>Richard Barwell.   |      |   |
| 1860 | William Ogle, M.D.<br>Thomas Bryant.<br>John Couper.  |      |   |
| 1861 | William Spencer Watson.   |      |   |
| 1862 | Lionel Smith Beale, M.B., F.R.S.<br>Edmund Symes Thompson, M.D.<br>Reginald Edward Thompson, M.D.<br>George Cowell. |      |   |
| 1863 | Sir Samuel Wilks, Bt., M.D., F.R.S.   |      |   |

- 1868 T. Henry Green, M.D.  
George Eastes.
- 1869 Joseph Frank Payne, M.D.  
Arthur E. Sansom, M.D.  
Thomas Laurence Read.
- 1870 J. Warrington Haward.  
Edgcombe Venning.  
Clement Godson, M.D.  
Reginald Harrison.  
Robert Leamon Bowles, M.D.
- 1871 William Cayley, M.D.  
Sir T. Lauder Brunton, M.D.,  
F.R.S.  
J. Hughlings Jackson, M.D., F.R.S.  
George Vivian Poore, M.D.  
Philip Frank, M.D.
- 1872 T. Gilbert-Smith, M.D.  
George B. Brodie, M.D.  
Sir J. Fayrer, M.D., F.R.S.  
Charles S. Tomes, M.A., F.R.S.  
Sir William Bartlett Dalby.
- 1873 Frederick Taylor, M.D.  
Norman Moore, M.D.  
Sir William R. Gowers, M.D., F.R.S.  
Jeremiah McCarthy.  
Wm. Johnson Smith.  
Alex. O. MacKellar.  
Henry T. Butlin.  
Charles Higgens.  
William J. Walsham.
- 1874 Alfred Lewis Galabin, M.D.  
George Thin, M.D.  
John Mitchell Bruce, M.D.  
Henry Morris, M.A.  
William Laidlaw Purves.  
William Harrison Cripps.  
Sir Henry G. Howse, M.S.  
Herbert William Page.  
Frederic Durham.  
William Robert Smith, M.D.
- 1875 Thomas T. Whipham, M.D.  
Thomas Crawford Hayes, M.D.  
Warren Tay.  
Edmund J. Spitta.  
Fletcher Beach, M.B.
- 1876 Sir Thomas Barlow, Bart., K.C.V.O.,  
M.D.  
Albert J. Venn, M.D.  
Sir Felix Semon, C.V.O., M.D.  
Sidney Coupland, M.D.  
Francis Warner, M.D.  
William Ewart, M.D.  
Alfred Pearce Gould, M.S.  
Rickman J. Godlee, M.S.
- 1877 Alban H. G. Doran.  
George Ernest Herman, M.B.  
Samuel West, M.D.  
John Abercrombie, M.D.  
George Allan Heron, M.D.  
Joseph A. Ormerod, M.D.  
P. Henry Pye-Smith, M.D., F.R.S.  
Sir William Henry Bennett,  
K.C.V.O.
- 1878 Sir Jas. Crichton-Browne, M.D.  
Fred. T. Roberts, M.D.  
Lord Lister, P.C., O.M., F.R.S.  
Clinton T. Dent.  
John H. Morgan, C.V.O.  
Donald W. Charles Hood, C.V.O.,  
M.D.
- 1879 Edward Woakes, M.D.  
Malcolm A. Morris.  
A. E. Cumberbatch.  
Edmund Owen.  
Arthur E. J. Barker.  
Sir Fredk. Treves, Bart., C.B.,  
K.C.V.O.  
Andrew Clark.  
Francis Henry Champneys, M.D.  
William Watson Cheyne, C.B.,  
F.R.S.  
George Henry Savage, M.D.  
H. H. Clutton, M.A.  
Frederic S. Eve.  
E. Noble Smith.  
William Henry Allechin, M.D.
- 1880 Robert Alex. Gibbons, M.D.  
David Ferrier, M.D., F.R.S.  
Vincent Dormer Harris, M.D.  
Edmund Distin Maddick.  
Jas. John MacWhirter Dunbar, M.D.  
James William Browne, M.B.  
William Appleton Meredith, M.B.  
Malcolm Macdonald McHardy.  
A. Boyce Barrow.  
William Murrell, M.D.  
George Ogilvie, M.B.  
Charles Edward Beevor, M.D.  
Thomas Colcott Fox, M.B.  
George Henry Makins, C.B.
- 1881 Francis de Havilland Hall, M.D.  
Robert Wharry, M.D.  
Richard Clement Lucas, B.S.  
Sir Stephen Mackenzie, M.D.  
William Hale White, M.D.  
Eustace Smith, M.D.  
Percy Kidd, M.D.  
Oswald A. Browne, M.D.

- 1881 W. Bruce Clarke, M.B.  
Dawson Williams, M.D.  
George Lindsay Johnson, M.D.  
Henry Edward Juler.  
Jonathan F. C. H. Macready.  
C. B. Lockwood.
- 1882 Philip J. Hensley, M.D.  
Ernest Clarke, M.D., B.S.  
George Robertson Turner.  
Howard Henry Tooth, C.M.G.,  
M.D.  
Sir Herbert Isambard Owen,  
M.D.  
Charles R. B. Keetley.  
Anthony A. Bowlby, C.M.G.  
Amand J. McC. Routh, M.D.  
Seymour J. Sharkey, M.D.  
William Lang.  
Henry Radcliffe Crocker, M.D.  
Sir James Reid, Bart., G.C.V.O.
- 1883 Edwin Clifford Beale, M.A., M.B.  
James Kingston Gowler, M.D.  
James Frederic Goodhart, M.D.  
W. Hamilton A. Jacobson, M.Ch.  
Walter H. Jessop, M.B.  
Walter Edmunds, M.C.  
Sir Victor A. Horsley, F.R.S.  
Dudley Wilmot Buxton, M.D.  
Charles Douglas F. Phillips, M.D.  
John James Pringle, M.B.  
Henry Roxburgh Fuller, M.D.  
Wilmot Parker Herringham, M.D.  
Augustus Waller, M.D.  
William Pasteur, M.D.  
John Bland-Sutton.  
Robert Marcus Gunn, M.B.
- 1884 George Newton Pitt, M.D.  
Charles Stonham, C.M.G.  
Stanley Boyd, B.S.  
William Arbuthnot Lane, M.S.  
Arthur Marmaduke Sheild, M.B.  
Sidney Harris Cox Martin, M.D.,  
F.R.S.  
Thomas Wakley, jun.  
F. Swinford Edwards.  
James Johnston, M.D.  
William Duncan, M.D.  
Charles Chinner Fuller.  
George Richard Turner Phillips.  
Bilton Pollard.
- 1885 Alexander Haig, M.D.  
Theodore Dyke Acland, M.D.  
Frederick Walker Mott, M.D., F.R.S.  
James Berry.
- 1885 John Cahill, M.D.  
John Poland.  
A. C. Butler-Smythe.  
Charles Alfred Ballance, M.S.  
Walter S. A. Griffith, M.D.  
John Edward Squire, M.D.  
John D. Malcolm, M.B., C.M.  
Phineas S. Abraham, M.D.
- 1886 Robert Maguire, M.D.  
Harrington Sainsbury, M.D.  
Cuthbert Hilton Golding-Bird, M.B.  
Lauriston Elgie Shaw, M.D.  
Charters James Symonds, M.S.  
Robert Boxall, M.D.  
Allan Ogier Ward, M.D.  
Archibald Edward Garrod, M.D.  
Stephen Paget.  
William Radford Dakin, M.D.  
Samuel Herbert Habershon, M.D.  
Arthur Quarry Silcock.  
Arthur H. N. Lewers, M.D.
- 1887 Walter George Spencer.  
Thomas Outterson Wood, M.D.  
Edgar William Willett, M.B.  
Henry Lewis Jones, M.D.  
Francis George Penrose, M.D.  
Hugh Percy Dunn.  
Frederic William Hewitt, M.V.O.,  
M.D.  
James Barry Ball, M.D.  
Gilbert Richardson, M.D.  
D'Arcy Power, M.B.  
John Gay.  
James Calvert, M.D.  
Percy J. F. Lush, M.B.  
Edward James Wallace, M.D.
- 1888 Robert Henry Scanes Spicer, M.D.  
Jonathan Hutchinson, jun.  
Campbell Williams.  
James Donelan, M.B., C.M.  
John Anderson, M.D., C.I.E.  
Laurie Asher Lawrence.  
Arthur Pearson Luff, M.D., B.Sc.  
Albert Carless, M.S.  
Frederick C. Wallis, M.B., B.C.  
Charles James Cullingworth, M.D.  
Edmund Cautley, M.D., B.C.  
H. Montague Murray, M.D.  
Frank Joseph Wethered, M.D.  
Edmund Wilkinson Roughton, B.S.  
Frederick William Cock, M.D.  
Robert Henry Clarke, M.B.  
Montagu Handfield-Jones, M.D.  
David Henry Goodsall.



- 1889 Raymond Johnson, M.B.  
 John Fletcher Little, M.B.  
 Henry Work Dodd.  
 George Lindsay Turnbull, M.D.  
 Sidney Phillips, M.D.  
 William Charles Bull, M.B.  
 George P. Field.  
 Henry Percy Dean, M.B., M.S.  
 Alfred Samuel Gubb, M.D.  
 William Hunter, M.D.  
 J. Inglis Parsons, M.D.  
 Bernard Pitts, M.B., M.C.  
 Robert Percy Smith, M.D., B.S.  
 Herbert R. Spencer, M.D., B.S.  
 Nestor Isidore Chas. Tirard, M.D.  
 Arthur William Mayo Robson.
- 1890 John Rose Bradford, M.D., F.R.S.  
 Charles D. B. Hale, M.D.  
 Sir Edwin Cooper Perry, M.D.  
 Morton Smale.  
 Frederick Willcocks, M.D.  
 William T. Holmes Spicer, M.B.  
 Thomas Henry Crowle.  
 Henry Walter Syers, M.D.  
 Seymour Taylor, M.D.  
 William Alfred Wills, M.D.  
 G. O. White-Cooper, M.B.  
 Herbert William Allingham.  
 William A. F. Bateman.  
 James Jackson Clarke, M.B.  
 Leonard G. Guthrie, M.D., B.Ch.  
 G. William Hill, M.D., B.Sc.  
 Edward Law, M.D., C.M.  
 Sir Patrick Manson, K.C.M.G.,  
 M.D., C.M., F.R.S.  
 Humphry D. Rolleston, M.D.  
 Arthur Henry Ward.  
 Walter Essex Wynter, M.D., B.S.  
 Edward Lawrie, M.B.  
 Christopher Childs, M.D.
- 1891 William Lee Dickinson, M.D.  
 Herbert P. Hawkins, M.D., B.Ch.  
 Cyril Ogle, M.A., M.B.  
 Arthur F. Voelcker, M.D., B.S.  
 Alfred Pownall Woodforde.  
 Herbert T. Herring, M.B., B.S.  
 Ernest Muirhead Little.  
 Henry Charrington Martin, M.D.  
 Frederick William Andrewes, M.D.  
 Alfred Eddowes, M.D.  
 Herbert Morley Fletcher, M.D.  
 William Heaton Hamer, M.D.  
 John Arthur Hayward, M.D.  
 William Bromfield Paterson.
- 1891 Holburt Jacob Waring.  
 Frederic Parkes Weber, M.D.  
 F. E. Batten, M.D.  
 Thomas Jessopp Bokenham.  
 Norman Dalton, M.D.  
 P. R. W. De Santi.  
 P. W. Dove.  
 William J. Gow, M.D.  
 Paul Frank Moline, M.B.  
 Edward Percy Paton, M.D.  
 Arthur Bowen Rendel, M.B., B.C.  
 James Samuel Risien Russell,  
 M.D.  
 Charles Percival White, M.B., B.C.  
 W. Page May, M.D.  
 Richard J. Reece.  
 Charles Ernest Baker, M.B.
- 1892 J. Dundas Grant, M.D.  
 R. J. Bliss Howard, M.D.  
 Thomas Horrocks Openshaw,  
 C.M.G., M.B.  
 William Bezly Thorne, M.D.  
 W. H. Russell Forsbrook, M.D.  
 John Harold, M.B.  
 John Alfred Masters, M.D.  
 Gustave Schorstein, M.B.  
 Charles Sempill de Segundo, M.B.  
 John Tweedy.  
 J. S. Selwyn-Harvey, M.D.  
 StClair Thomson, M.D.  
 Henry Rayner, M.D.  
 H. Marmaduke Page.  
 Almroth Edward Wright, M.D.
- 1893 James Taylor, M.D.  
 Howard Barrett.  
 Robert Cozens Bailey, M.B.  
 Henry Albert Caley, M.D.  
 Arthur Edward Giles, M.D.  
 Miles Miley, M.B.  
 D. Watkin Roberts, M.D.  
 Leonard A. Bidwell.  
 Frédéric F. Burghard, M.D., M.S.  
 J. H. Drysdale, M.B.  
 William McAdam Eccles, M.S.  
 Vaughan Harley, M.D.  
 George Herschell, M.D.  
 Arnold Lawson.  
 Guthrie Rankin, M.D.
- 1894 Richard Gill.  
 Joseph Sefton Sewill.  
 Thomas Vincent Dickinson, M.D.  
 Alexander Morison, M.D.  
 L. Hemington Pegler, M.D.  
 Herbt. Furnivall Waterhouse, C.M

- 1894 Percy Furnivall.  
R. L. Langdon-Down, M.B., B.C.  
Allan Macfadyen, M.D., B.S.  
Ernst Michels, M.D.  
Wm. Rivers Pollock, M.B., B.C.  
Charles Slater, M.B.  
G. H. Ward-Humphreys.
- 1895 Charles Arthur Parker.  
Sydney Russell Wells, M.D.  
Alfred Milne Gossage, M.B.  
Robert Murray Leslie, M.B.  
James Galloway, M.D.  
David Bridge Lees, M.D.  
Arthur G. Phear, M.D.  
Edward Erskine Henderson, M.B.
- 1896 Joseph Lockhart Downes, M.B.  
Edward Wilberforce Goodall, M.D.  
James Ernest Lane.  
George Alex. Sutherland, M.D.  
Charles Buttar, M.D.  
P. J. Freyer, M.D., I.M.S., M.A.  
Percival Horton-Smith, M.D.  
James Keogh Murphy, M.B.  
Thomas William Shore, M.D.  
William Aldren Turner, M.D.  
Charles Hubert Roberts, M.D.  
Charles R. J. Atkin Swan, M.B.  
James Kingston Barton.  
J. Walter Carr, M.D.  
John H. Dauber, M.A., M.B., B.Ch.  
Alexander Grant Russell Foulerton.  
L. Vernon Jones, B.A., M.D., B.Ch.  
Henry Betham Robinson, M.S.  
Horace George Turney, M.D.  
Ernest Waggett, M.B., B.C.  
Frederick Joseph Waldo, M.D.  
Hugh Walsham, M.D.  
J. W. W. Stephens, M.D.  
William Edward Lee, M.D.
- 1897 Comyns Berkeley, M.B., B.C.  
William Arthur Brailey, M.D.  
James Cantlie, M.B.  
Raymond H. Payne Crawford, M.D.  
Louis Jenner, M.B.  
Francis Whittaker Tunncliffe, M.D.  
Arthur Whitfield, M.D.  
Edward Stainer, M.A., M.B.  
Alfred G. Levy, M.D.  
A. P. Beddard, M.B.  
G. F. Blacker, M.D.  
W. S. Colman, M.D.  
F. W. Goodbody, M.D.  
R. Hutchison, M.D.  
Harold Low.
- 1897 Christopher Addison, M.D.  
Charles Powell White.
- 1898 J. H. Bryant, M.D.  
W. H. Corfield, M.D.  
L. A. Dunn, M.S.  
E. Hurry Fenwick.  
Sir A. Downing Fripp, C.B.,  
M.V.O., M.S.  
A. Corrie Keep, M.D.  
A. C. Latham, M.D.  
J. B. Lawford.  
John McFadyean.  
H. Murray Ramsay.  
J. F. H. Broadbent, M.D.  
H. Ronald Carter.  
A. Stark Currie, M.D.  
James Morrison, M.D.  
J. S. Edkins, M.B.  
Thomas J. Horder, M.D.  
F. W. Robertson.  
S. Jervois Aarons, M.D.  
Willmott Evans, M.D., B.S., B.Sc.  
John Murray.  
W. Adams Frost.  
C. R. C. Lyster.  
Samuel Noble Bruce.  
Cuthbert Chapman Gibbes, M.D.  
H. Stringfellow Pendlebury, M.B.  
William Turner, M.B.  
Alexander Crombie, C.B., M.D.  
Thomas Herbert Kellock, M.D.
- 1899 James Hugh Thursfield, M.D.  
Lindley Marcroft Scott, M.D.  
Alfred P. Hillier, M.D.  
Louis Bathe Rawling, M.B.  
John Edward Sandilands, M.B.  
Arthur J. Whiting, M.D.  
Edward Farquhar Buzzard, M.D.  
Greville Macdonald, M.D.  
George Jones, M.B.  
Herbert Campbell Thomson, M.D.  
Thomas Morison Legge, M.D.  
William John Ritchie Simpson,  
M.D.  
Ernest Playfair, M.B.  
Karl Fürth, M.D.  
Purves Stewart, M.D.
- 1900 Clive Riviere, M.D.  
H. Roe Walker.  
Richard Lake.  
Percy Flemming, M.D., B.S.  
John Shields Fairbairn, M.B.,  
B.Ch.  
Aslett Baldwin.

- |   |  |
|---|--|
| <p>1900 Charles Ryall.<br/>William Hern.<br/>Cecil Huntington Leaf, M.B.<br/>Edwin Harding Lendon, M.D.<br/>Lieut.-Col. William Reid Murphy,<br/>D.S.O., I.M.S.<br/>James Harry Sequeira, M.D.<br/>Harold Batty Shaw, M.D.<br/>Charles Herbert Thompson, M.D.<br/>John William Thomson-Walker.</p> <p>1901 Sir Hugh Reeve Beevor, Bart.,<br/>M.D.<br/>J. Brunton Blaikie, M.D.<br/>John Patrick Henry, M.D.<br/>Herbert John Paterson.<br/>George Henkell Drummond Robin-<br/>son, M.D.<br/>Elmore Wright Brewerton.<br/>Thomas Rupert Hampden Bucknall,<br/>M.S., M.D.<br/>William Douglas Harmer.<br/>Harry George Plimmer.<br/>Lionel Vernon Cargill.<br/>T. N. Kelynack, M.D.<br/>Leonard Williams, M.D.</p> <p>1902 J. P. Lockhart Mummery, B.A.<br/>James Stansfield Collier, M.D.,<br/>B.Sc.</p> | <p>1902 Robert Salusbury Trevor, M.B., B.C.<br/>Edward Arthur Saunders, M.B.,<br/>B.Ch.<br/>Ralph Vincent, M.D., B.C.<br/>Herbert French, M.B.<br/>Holland John Cotton, M.D., C.M.<br/>Arthur Evans, M.S.<br/>James Kerr, M.D., D.P.H.<br/>Donald John Armour, M.B.<br/>David Barty King, M.D., Ch.B.<br/>Hector William Gavin Mackenzie,<br/>M.D.<br/>John Abernethy Willett, M.B.<br/>Thomas Crisp English.<br/>Louis W. Sambon, M.D.<br/>Joseph Blumfield, M.D., B.C.<br/>Ernest Beddoe Hulbert, M.D.<br/>Harold L. Barnard, M.S.<br/>Fallon Percy Wightwick, M.D.</p> <p>1903 Edmund Ivens Spriggs, M.D.<br/>Otto F. F. Grünbaum, M.B., B.C.<br/>Samuel William Carruthers, M.D.<br/>John Russell Ryan, M.D., B.Ch.<br/>Oliver K. Williamson, M.D.<br/>Herbert Louis Powell Hulbert.<br/>William Lawrence Ascherson,<br/>M.B., B.C.<br/>Eustace Talbot, M.B.</p> |
|---|--|

**The following Non-resident Fellows pay an annual subscription of £3 3s., and are thereby entitled to all the privileges of Resident Fellows.**

***Elected***

- 1900 BLAKE, WILLIAM HENRY, M.D.Brux., Bedford Lodge,  
West Wickham, Kent.
- 1884 DRAGE, LOVELL, M.D., B.Ch.Oxon., Burleigh Mead,  
Hatfield, Herts.
- 1897 GILFORD, HASTINGS, Norwood House, King's road,  
Reading. *Trans.* 1.
- 1900 PRICE-JONES, CECIL, M.B., 7, Claremont road, Surbiton,  
Surrey.
- 1882 REID, THOMAS WHITEHEAD, M.D., Surgeon to the Kent  
and Canterbury Hospital; St. George's House, Canter-  
bury.
- 1891 RUFFER, MARC ARMAND, M.D., The Quarantine Board,  
Alexandria.
- 1898 THOMAS, J. LYNN, C.B., Surgeon to the Cardiff Infirmary;  
Consulting Surgeon to the Hamadryad Hospital,  
Green-lawn, Pen-y-Lan, Cardiff.

## NON-RESIDENT FELLOWS

### *Elected*

- 1866 *ALLBUTT, THOMAS CLIFFORD*, M.D., LL.D. Glasgow, F.R.S.,  
Regius Professor of Physic, University of Cambridge ;  
Consulting Physician to the Leeds General Infirmary ;  
St. Rhadegund's, Cambridge. *Trans.* 4.
- 1884 *ANDERSON, ALEXANDER RICHARD*, Surgeon to the General  
Hospital, 5, East Circus Street, Nottingham. *Trans.* 1.
- 1880 *Appleton, HENRY*, M.D. (Address uncommunicated.)
- 1896 *BAGSHAW, FREDERIC*, M.D., J.P., 35, Warrior Square, St.  
Leonard's-on-Sea.
- 1902 *BAILLY, WILLIAM HENRY*, M.B., Featherstone Hall,  
Southall, Middlesex.
- 1895 *BALDWIN, GERALD R.*, 166, Victoria street, Melbourne,  
Australia.
- 1891 *BALGARNIE, WILFRED*, M.B., The Dutch House, Hartley  
Wintney, Winchfield.
- 1896 *BALL, SIR CHARLES BENT*, M.D., Ch.M., 24, Merrion  
square North, Dublin.
- 1866 *Banks, SIR JOHN*, K.C.B., M.D., LL.D., D.Sc., Physician  
in Ordinary to H.M. the King in Ireland ; Physician  
to Richmond, Whitworth, and Hardwicke Hospitals ;  
Regius Professor of Physic in the University of Dublin ;  
45, Merrion square, Dublin.
- 1886 *BANKS, SIR WILLIAM MITCHELL*, M.D., Surgeon to the  
Liverpool Royal Infirmary ; 28, Rodney street, Liver-  
pool.

*Elected*

- 1900 *BARDSWELL, NOEL DEAN*, M.D., The Sanatorium, Mundesley, Norfolk.
- 1882 *BARKER, FREDERICK CHARLES*, M.D., Surgeon-Major, Bombay Medical Service.
- 1881 *BARNES, HENRY*, M.D., LL.D., F.R.S. Ed., Physician to the Cumberland Infirmary; 6, Portland square, Carlisle.
- 1861 *BARNES, ROBERT*, M.D., Bernersmede, Eastbourne. C. 1877-8. V.P. 1889-90. *Referee*, 1867-76, 1891-6. *Lib. Com.* 1869-73. *Sci. Com.* 1889-1902. *Trans.* 4.
- 1860 *BEALEY, ADAM*, M.D., M.A., Felsham Lodge, Felsham road, St. Leonard's-on-Sea, Sussex.
- 1896 *BELBEN, FRANK*, M.B., Endsleigh, Suffolk road, Bourne-mouth.
- 1880 *BENNETT, ALEXANDER HUGHES*, M.D. (Travelling.)
- 1889 *BENTLEY, ARTHUR J. M.*, M.D., Mena House, Pyramids, Cairo, Egypt.
- 1872 *BEVERLEY, MICHAEL*, M.D., Consulting Surgeon to the Norfolk and Norwich Hospital; 54, Prince of Wales road, Norwich.
- 1865 *BICKERSTETH, EDWARD ROBERT*, Consulting Surgeon to the Liverpool Royal Infirmary; 2, Rodney street, Liverpool. *Trans.* 1.
- 1892 *BICKERSTETH, ROBERT ALEXANDER*, M.A., M.B., Assistant Surgeon to the Liverpool Royal Infirmary: 2, Rodney street, Liverpool.
- 1901 *BISSHOPP, FRANCIS R. B.*, M.D., Belle Vue, Mount Pleasant, Tunbridge Wells.
- 1900 *BLAKE, WILLIAM HENRY*, M.D.Brux., Bedford Lodge, West Wickham, Kent.
- 1865 *BLANCHET, HILARION*, 35, Conillard street, Quebec, Canada.
- 1890 *BOSTOCK, R. ASHTON*, Surgeon, Scots Guards, Cefn Mor, Penmaen, Glamorganshire.
- 1869 *BOURNE, WALTER*, M.D. (Travelling.)

*Elected*

- 1874 *BRADSHAW, A. F.*, C.B., Surgeon Major-General, 111, Banbury road, Oxford.
- 1899 *BRADSHAW, THOMAS ROBERT*, M.D., 51, Rodney street, Liverpool. *Trans.* 2.
- 1900 *BRAINE-HARTNELL, JAMES CHRISTOPHER REGINALD*, Cotswold Sanatorium, Stroud, Glos.
- 1899 *BREMIDGE, RICHARD HARDING*, Mysore, India (c/o R. Bremridge, 17, Bloomsbury square).
- 1876 *BRIDGES, ROBERT*, M.B., Manor House, Yattendon, Newbury, Berks.
- 1867 *BRIDGEWATER, THOMAS*, M.B., LL.D., Harrow-on-the-Hill, Middlesex.
- 1891 *BRODIE, CHARLES GORDON*, Fernhill, Wootton Bridge, Isle of Wight.
- 1892 *BRONNER, ADOLPH*, M.D., Senior Surgeon to Bradford Eye and Ear Hospital; Laryngologist to Bradford Royal Infirmary; 33, Manor row, Bradford.
- 1894 *BROOK, WILLIAM HENRY BREEFIT*, M.D., B.S., 8, Eastgate, Lincoln.
- 1899 *BROOKSBANK, HUGH LAMPLUGH*, M.B., B.C., 5, College road, Windermere.
- 1888 *BROWNE, HENRY LANGLEY*, Moor House, West Bromwich.
- 1881 *BROWNE, JOHN WALTON*, M.D., Surgeon to the Belfast Royal Hospital; Surgeon to the Belfast Ophthalmic Hospital; 10, College square N., Belfast.
- 1864 *BUCKLE, FLEETWOOD*, M.D., Merton Lodge, Merton road, Southsea.
- 1901 *BYRNE, WILLIAM SAMUEL*, M.D., Anne street, Brisbane, Queensland.
- 1891 *Campbell, HENRY JOHNSTONE*, M.D., 36, Manningham lane, Bradford.
- 1900 *CARLYON, THOMAS BAXTER*, 6, Marine place, Dover.
- 1888 *CARTER, WILLIAM JEFFREYS BECHER*, Aliwal North, Cape Colony.

*Elected*

- 1898 *CAYE, EDWARD JOHN*, M.D., Bath.
- 1884 *CHAPPEY, WAYLAND CHARLES*, M.D., Physician to the Royal Alexandra Hospital for Children; 13, Montpelier road, Brighton.
- 1885 *CHAPMAN, PAUL MORGAN*, M.D., Physician to the Hereford General Infirmary, 1, St. John street, Hereford. *Trans.* 1.
- 1881 *Chavasse, THOMAS FREDERICK*, M.D., C.M., Senior Surgeon to the Birmingham General Hospital; 22, Temple row, Birmingham. *Trans.* 3.
- 1873 *Chisholm, EDWIN*, M.D., 44, Rosslyn gardens, Darlinghurst, Sydney, New South Wales.
- 1896 *CHRISTOPHERSON, JOHN BRIAN*, M.D., B.C., late Assistant Demonstrator of Anatomy at St. Bartholomew's Hospital; late Surgeon to Seamen's Hospital, Albert Dock; c/o P.M.O., Egyptian Army, Cairo.
- 1892 *CLARK, JAMES CHARLES*, 35, Castle road, Bedford.
- 1897 *CLARK, W. GLADSTONE*, Civil Service Club, Capetown.
- 1857 *COATES, CHARLES*, M.D., Consulting Physician to the Bath Royal United Hospital; 10, Circus, Bath.
- 1893 *COLE, ROBERT HENRY*, M.D., Moorcroft, Hillingdon, Uxbridge.
- 1891 *COOK, HERBERT GEORGE*, M.D., B.S., 22, Newport road, Cardiff.
- 1899 *CORRIGAN, WILLIAM JENKINSON*, Cloughmore, Splott avenue, Cardiff.
- 1891 *COUNBE, JOHN BATTEN*, M.D., 64, Caeran road, Newport, Mon.
- 1869 *Cresswell, PEARSON R.*, C.B., Senior Surgeon to the Merthyr General Hospital; Dowlais, Merthyr Tydfil.
- 1892 *CROSS, FRANCIS RICHARDSON*, M.B., Ophthalmic Surgeon to the Bristol Royal Infirmary, and Surgeon to the Bristol Eye Hospital; Worcester House, Clifton, Bristol.
- 1895 *DARDEL, JEAN*, M.D., Aix-les-Bains, Savoy.



*Elected*

- 1879 *DARWIN FRANCIS*, M.B., F.R.S., Wychfield, Huntingdon road, Cambridge.
- 1874 *DAVIDSON, ALEXANDER*, M.D., Consulting Physician to the Liverpool Royal Infirmary; Emeritus Professor, University College, Liverpool; 2, Gambier terrace, Liverpool.
- 1878 *DAVY, RICHARD*, Consulting Surgeon to the Westminster Hospital; Burstone House, Bow, North Devon. *Trans.* 1.
- 1882 *DAWSON, YELVETON*, M.D., Heathlands, Southbourne-on-Sea, Hants.
- 1889 *DELEPINE, SHERIDAN*, B.Sc., M.B., C.M., Professor of Pathology, Owens College, Manchester. *Trans.* 1.
- 1899 *DOUGLAS, ARCHIBALD ROBERT JOHN*, M.B., B.S., c/o Watson & Co., 7, Waterloo place, S.W.
- 1902 *DOUTY, E. H.*, M.D., Davos, Switzerland.
- 1867 *DRAKE, CHARLES*, M.D., Hatfield, Herts.
- 1884 *DRAKE, LOVELL*, M.D.Oxon., Burleigh Mead, Hatfield, Herts.
- 1898 *DRESCHFELD, JULIUS*, Farndon House, Rusholme, Manchester.
- 1885 *DRUMMOND, DAVID*, M.D., 7, Saville place, Newcastle-on-Tyne.
- 1880 *DEURY, CHARLES DENNIS HILL*, M.D., Bondgate, Darlington.
- 1899 *DRURY, EDWARD GUY DRU*, M.B., B.S., Grahamstown, South Africa.
- 1871 *DUKES, CLEMENT*, M.D., B.S., Physician to Rugby School, and Senior Physician to the Hospital of St. Cross, Rugby; Sunnyside, Rugby, Warwickshire.
- 1867 *DUKES, MAJOR CHARLES*, M.D., Clarence Villa, Torrs park, Ilfracombe, North Devon.
- 1889 *DUNCAN, JOHN*, M.D., St. Petersburg, Russia.
- 1894 *DURHAM, HERBERT EDWARD*, M.B., Pathological Laboratory, Cambridge. *Trans.* 2.

*Elected*

- 1872 *EAGER, REGINALD*, M.D., Northwoods, near Bristol.
- 1887 *EASMON, JOHN FARRELL*, M.D., Assistant Colonial Surgeon, Gold Coast Colony, and Acting Chief Medical Officer of the Colony; Accra, Gold Coast, West Africa.
- 1887 *ELLIOTT, JOHN*, 24, Nicholas street, Chester.
- 1868 *ELLIS, JAMES*, M.D., The Sanatorium, Anaheim, Los Angeles County, California.
- 1889 *ELLISTON, WILLIAM ALFRED*, M.D., Stoke Hall, Ipswich.
- 1875 *Fagan, JOHN*, Consulting Surgeon to the Belfast Royal Hospital; 20, Fitzwilliam place, Dublin.
- 1897 *FAGGE, THOMAS HENRY*, M.D., Villa de la Porte Rouge, Monte Carlo.
- 1869 *FAIRBANK, FREDERICK ROYSTON*, M.D., Westcott, Dorking.
- 1902 *FENNELL, CHARLES HENRY*, M.A., M.D., Darenth Asylum, Dartford, Kent.
- 1872 *Fenwick, JOHN C. J.*, M.D., Physician to the Durham County Hospital; Long Framlington, Morpeth.
- 1879 *FINLAY, DAVID WHITE*, M.D., Professor of the Practice of Medicine in the University of Aberdeen; Physician and Lecturer on Clinical Medicine to the Aberdeen Royal Infirmary; Consulting Physician to the Royal Hospital for Diseases of the Chest, London; 2, Queen's terrace, Aberdeen. *Referee*, 1891-3. *Trans.* 2.
- 1864 *Folker, WILLIAM HENRY*, Consulting and late Hon. Surgeon to the North Staffordshire Infirmary; Bedford House, Hanley, Staffordshire.
- 1896 *FORESTIER, HENRI*, M.D., Aix-les-Bains, Savoie, France.
- 1892 *FOSTER, MICHAEL GEORGE*, M.A., M.D., Villa Camilla, San Remo.
- 1884 *Franks, KENDAL*, M.D., c/o J. H. Franks, Esq., C.B., Dalriada, Blackrock, co. Dublin. *Trans.* 2.
- 1903 *Freeborn, JOHN C. R.*, 38, Broad street, Oxford.
- 1876 *FURNEE, WILLOUGHBY*, M.D., Surgeon to the Sussex County Hospital; Brunswick square, Brighton.

*Elected*

- 1864 *Gairdner, SIR WILLIAM TENNANT*, M.D., K.C.B., LL.D., F.R.S., Honorary Physician in Ordinary to H.M. the King in Scotland; formerly Professor of the Practice of Medicine in the University of Glasgow; Honorary Consulting Physician to the Western Infirmary, Glasgow; 32, George square, Edinburgh. *Trans.* 1.
- 1885 *GANGEE, ARTHUR*, M.D., LL.D., F.R.S., Emeritus Professor of Physiology in the Owens College, Victoria University, Manchester; Montreux, Switzerland.
- 1867 *GARLAND, EDWARD CHARLES*, Yeovil, Somerset.
- 1879 *GARSTANG, THOMAS WALTER HARROPP*, Englefield, Delamer road, Bowdon, Cheshire.
- 1889 *Gaskell, WALTER HOLBROOK*, M.D., F.R.S., Lecturer on Physiology, University of Cambridge; The Uplands, Great Shelford, Cambs.
- 1884 *GIBBES, HENEAGE*, M.D., Health Officer, Detroit, Michigan, U.S.A.
- 1897 *GIBSON, GEORGE ALEXANDER*, M.D., D.Sc., 3, Drumsheugh Gardens, Edinburgh.
- 1897 *GILFORD, HASTINGS*, Norwood House, King's road, Reading. *Trans.* 2.
- 1893 *GORDON, WILLIAM*, M.B., M.C., The Old Rectory, Goring-on-Thames, Oxon.
- 1890 *Gordon, WILLIAM*, M.D., Barnfield Lodge, Exeter.
- 1898 *GRANVILLE, ALEXANDER*, Turf Club, Cairo.
- 1898 *GRAY, J. A.*, M.B., Wadham Lodge, Uxbridge road, Ealing.
- 1889 *GREENE, GEORGE EDWARD JOSEPH*, M.A., D.Sc., F.L.S., Monte Vista, Ferns, County Wexford.
- 1875 *Greenfield, WILLIAM SMITH*, M.D., Professor of Pathology and Clinical Medicine in the University of Edinburgh; 7, Heriot row, Edinburgh. *Sci. Com.* 1879. *Referee*, 1881.
- 1900 *GREER, WILLIAM JONES*, 2, Chepstow road, Newport, Mon.
- 1882 *GRESSWELL, DAN ASTLEY*, M.A., M.D., D.P.H., Chairman, Board of Public Health, Melbourne, Victoria.

*Elected*

- 1889 **GRIFFITHS, JOSEPH, M.A., M.D., C.M.**, Reader in Surgery in the University of Cambridge; Surgeon to Addenbrooke's Hospital; 63, Trumpington street, Cambridge. *Pro.* 1.
- 1870 **HAMILTON, ROBERT**, Consulting Surgeon to the Royal Southern Hospital, Liverpool; Magherabuoy, Portrush, co. Antrim, Ireland.
- 1864 **HARLEY, JOHN, M.D., F.L.S.**, Hon. Physician to St. Thomas's Hospital; Consulting Physician to the London Fever Hospital; Beeding, Pulborough, Sussex. S. 1875-7. C. 1879-80. V.P. 1895-7. *Referee*, 1871-4, 1882-95. *Sci. Com.* 1879. *Trans.* 10.
- 1901 **HARTIGAN, T. J. P.**, "Heathcote," East Grinstead, Sussex.
- 1890 **HAVILAND, FRANK PAPILLON, M.D., B.C.**, 57, Warrior square, St. Leonard's-on-Sea.
- 1885 **HAWKINS, FRANCIS HENRY, M.D.**, Physician to the Royal Berkshire Hospital; 73, London street, Reading. *Trans.* 1.
- 1900 **HAYFORD, ERNEST JAMES, M.D.**, c/o The Agent, Claude's Ashanti Goldfields, Limited, Cape Coast Castle, Gold Coast.
- 1860 **HAYWARD, HENRY HOWARD**, Consulting Surgeon Dentist to St. Mary's Hospital; Harbledown, 120, Queen's road, Richmond. C. 1878-9.
- 1899 **HIND, HENRY**, Harrogate.
- 1900 **HOBHOUSE, EDMUND, M.D.**, 36, Brunswick place, Brighton.
- 1843 **HOLDEN, LUTHER**, Consulting Surgeon to St. Bartholomew's Hospital, Pinetoft, Ipswich. C. 1859. L. 1865. V.P. 1874. *Referee*, 1866-7. *Lib. Com.* 1858.
- 1894 **HOLLAND, JAMES FRANK, M.D.**, St. Moritz, Engadine, Switzerland.

*Elected*

- 1868 *HOLLIS, WILLIAM AINSLIE*, M.D., Physician to the Sussex County Hospital ; 1, Palmeira avenue, Hove. *Trans.* 1.
- 1881 *HOWARD, HENRY*, M.B., Medical Officer of Health, Williamstown, Melbourne, Victoria.
- 1898 *HULKE, S. BACKHOUSE*, Ivy House, Walmer, Kent.
- 1882 *HUMPHRY, LAURENCE*, M.D., 3, Trinity street, Cambridge.
- 1847 *IMAGE, WILLIAM EDMUND*, Herringswell House, Mildenhall, Suffolk. *Trans.* 1.
- 1883 *Jenkins, EDWARD JOHNSTONE*, M.D., The Australian Club, Sydney, New South Wales.
- 1881 *JENNINGS, WILLIAM OSCAR*, M.D., 74, Avenue Marceau, Paris.
- 1901 *JOHNSON, EDWARD ANGAS*, M.B., St. Catharine's, Prospect, South Australia.
- 1889 *JOHNSON, HAROLD J.*, Senior Assistant, Gloucester County Asylum, Gloucester.
- 1876 *JONES, LESLIE HUDSON*, M.D., Limefield House, Cheetham hill, Manchester.
- 1875 *Jones, PHILIP SYDNEY*, M.D., Consulting Surgeon to the Sydney Infirmary ; 10, College street, Sydney, New South Wales. [Agents: Messrs. D. Jones & Co., Wool Exchange, Coleman Street, E.C.]
- 1865 *JORDAN, FURNEAUX*, Consulting Surgeon to the Queen's Hospital, Birmingham ; Harborne, near Birmingham.
- 1872 *KELLY, CHARLES*, M.D., Ellesmere, Gratwicke road, Worthing, Sussex.
- 1890 *Kerr, J. G. DOUGLAS*, M.B., C.M., 6, The Circus, Bath.
- 1884 *KESER, JEAN SAMUEL*, M.D., Villa Colatel, Chemin Vinet, Lausanne, Switzerland.

*Elected*

- 1877 *Khory, RUSTOMJEE NASERWANJEE*, M.D.Brux., Hormazd Villa, Khumballa hill, Bombay.
- 1898 *KLEFSTAD-SILLONVILLE, O.*, M.D., Aix-les-Bains, Savoie.
- 1888 *KINSEY, SIR WILLIAM RAYMOND*, C.M.G., Westfield, Catherine road, Surbiton. (Travelling.)
- 1889 *LANCASTER, ERNEST LE CRONIER*, M.B., B.Ch., Assistant Physician to the Swansea Hospital; Hon. Physician to the Swansea and South Wales Institution for the Blind; Winchester House, Swansea, S. Wales.
- 1873 *Larcher, O.*, M.D., Laureate of the Institute of France, of the Medical Faculty, and Academy of Paris, &c.; 97, Rue de Passy, Passy, Paris.
- 1862 *LATHAM, PETER WALLWORK*, M.D., Downing Professor of Medicine, Cambridge University, 1874-94; Senior Physician to Addenbrooke's Hospital, Cambridge; 17, Trumpington street, Cambridge.
- 1880 *LAYCOCK, GEORGE LOCKWOOD*, M.B., C.M., Melbourne Victoria, Australia.
- 1892 *LAZARUS-BARLOW, WALTER SYDNEY*, M.D., Cecil House, Cavendish road, Sutton, Surrey. *Sci. Com.* 1892-1902.
- 1886 *Lediard, HENRY AMBROSE*, M.D., Surgeon to the Cumberland Infirmary; 35, Lowther street, Carlisle. *Trans.* 1.
- 1882 *LEDWICH, EDWARD L'ESTRANGE*, Anatomist to the Royal College of Surgeons, Ireland; 80, Upper Fitzwilliam street, Dublin.
- 1883 *LEESON, JOHN RUDD*, M.D., C.M., Clifden House, Twickenham.
- 1869 *LEGG, JOHN WICKHAM*, M.D. C. 1886. *Referee*, 1882-5. *Lib. Com.* 1878-85. *Trans.* 2.
- 1898 *LINDSAY, JAMES*, M.A., M.D., 13, College square East, Belfast.

*Elected*

- 1889 *LITTLE, JAMES*, M.D., Physician to the Adelaide Hospital; 14, Stephen's Green North, Dublin.
- 1894 *LOWE, THOMAS PAGAN*, 16, The Circus, Bath.
- 1889 *MACALISTER, DONALD*, M.A., B.Sc., M.D., Physician to Addenbrooke's Hospital; Linacre Lecturer and Tutor, St. John's College; University Lecturer in Medicine St. John's College, Cambridge.
- 1887 *MACDONALD, GEORGE CHILDS*, M.D. (Address uncommunicated.)
- 1866 *MAGGOWAN, ALEXANDER THORBURN*, M.D., Vyvian House, Clifton park, Bristol.
- 1876 *MACKAY, EDWARD*, M.D., Physician to the Sussex County Hospital; Senior Physician to the Royal Alexandra Hospital for Sick Children; 56, Lansdowne place, Brighton.
- 1854 *Mackinder, DRAPER*, M.D., 12, Park View Villas, Hove, Sussex.
- 1893 *MACLEOD, SURGEON-COLONEL KENNETH*, M.D., The Towers, Woolston, S. Hants.
- 1876 *MACNAMARA, N. CHARLES*, Consulting Surgeon to the Westminster Hospital, and to the Royal Westminster Ophthalmic Hospital; The Lodge, Chorley Wood. C. 1891-2. V.P. 1902—. *Referee*, 1884-90, 1895-7. *Lib. Com.* 1886-90.
- 1891 *MANBY, ALAN REEVE*, M.V.O., M.D., Surgeon Apothecary to His Majesty's Household at Sandringham and to T.R.H. the Prince and Princess of Wales at Sandringham; East Rudham, Norfolk.
- 1894 *MARRIOTT, CHARLES WILLIAM*, M.D., Aubrey House, Bath road, Reading.
- 1892 *MARTIN, CHRISTOPHER*, M.B., C.M., Surgeon to the Birmingham and Midland Hospital for Women; 35, George road, Edgbaston, Birmingham.
- 1899 *MARTIN, GILBERT JOHN KING*, M.D., 8, Gay street, Bath.

*Elected*

- 1883 *MAUDSLEY, HENRY CARE*, M.D., 22, Collins street, Melbourne, Victoria.
- 1889 *MEADE, RICHARD HENRY*, Consulting Surgeon to the Bradford Infirmary; Bradford, Yorkshire. *Trans.* 1.
- 1897 *MERRY, WILLIAM JOSEPH COLLINGS*, M.D., B.Ch., 2, Chiswick place, Eastbourne.
- 1898 *Millard, WILLIAM JOSEPH KELSON*, M.D., 7, Bayshill villas, Cheltenham.
- 1895 *MILLS-ROBERTS, ROBERT HERBERT*, Hafod-ty, Llanberis, North Wales.
- 1896 *MOORE, SIR JOHN*, M.D., 40, Fitzwilliamsquare west, Dublin.
- 1891 *MORRIS, GRAHAM*, Wallington, Surrey.
- 1894 *MORSE, THOMAS HERBERT*, All Saints' Green, Norwich. *Trans.* 1.
- 1902 *MOYNIHAN, BERKELEY GEORGE ANDREW*, M.S., 33, Park square, Leeds. *Trans.* 1.
- 1899 *MUNDY, HERBERT*, Kennington, Oxford (c/o Fleming Johnston, 460, West Street, Durban).
- 1892 *MYDDELTON-GAVEY, E. HERBERT*, 16, Broadwater Down, Tunbridge Wells.
- 1881 *NALL, SAMUEL*, M.B., Dryhurst Lodge, Disley, Stockport.
- 1889 *NAPIER, FRANCIS HORATIO*, M.B., Cape Town.
- 1870 *NEILD, JAMES EDWARD*, M.D., Lecturer on Forensic Medicine and Psychological Medicine in the University of Melbourne; 21, Spring street, Melbourne, Victoria.
- 1902 *Newland, HENRY SIMPSON*, M.B., Ch.B., Adelaide, South Australia.
- 1895 *NEWSHOLME, ARTHUR*, M.D., 11, Gloucester place, Brighton.
- 1868 *NICHOLLS, JAMES*, M.D., Trekenning House, St. Columb, Cornwall.
- 1847 *Nourse, WILLIAM EDWARD CHARLES*, Norfolk Lodge, Thurloe road, Torquay.



*Elected*

- 1880 O'CONNOR, BERNARD, A.B., M.D., Senior Physician to the North London Hospital for Consumption; 25, Hamilton road. Ealing.
- 1855 Ogle, WILLIAM, M.A., M.D., Consulting Physician to the Royal Derbyshire Infirmary; The Elms, Duffield road, Derby.
- 1870 OLDHAM, CHARLES FREDERIC, India [Agents: Messrs. Grindlay and Co., 55, Parliament street].
- 1896 OLIVER, GEORGE, M.D., Riversleigh, Farnham, Surrey, and Harrogate.
- 1883 Oliver, THOMAS, M.A., M.D., Professor of Physiology, University of Durham; and Physician to the Newcastle-on-Tyne Infirmary; 7, Ellison place, Newcastle-on-Tyne. *Trans.* 1.
- 1871 O'Neill, WILLIAM, M.D., C.M., late Physician to the Lincoln Lunatic Hospital, and Physician, Lincoln General Dispensary, &c.; 2, Lindum road, Lincoln.
- 1890 ORD, WILLIAM WALLIS, M.D., The Hall, Salisbury.
- 1885 ORMSBY, L. HEPENSTAL, M.D., Lecturer on Clinical and Operative Surgery and Surgeon to the Meath Hospital and County Dublin Infirmary; Surgeon to the Children's Hospital, Dublin; 92, Merrion square West, Dublin.
- 1894 OSBORN, SAMUEL, Knight of Grace of St. John; Maisonnnette, Datchet, Bucks.
- 1887 PAGET, CHARLES EDWARD, Medical Officer of Health to the County Council of Northamptonshire; County Hall, Northampton.
- 1858 Paley, WILLIAM, M.D., Physician to the Ripon Dispensary; Yore Bank, Ripon, Yorkshire.
- 1887 PARINGTON, GEORGE LUCAS, M.D., 47, Mount Pleasant road, Tunbridge Wells.

*Elected*

- 1873 *PARKER, ROBERT WILLIAM*, Consulting, late Senior Surgeon to the East London Hospital for Children and to the German Hospital; Caryll Hurst, West Grinstead, Sussex. C. 1888-9, 1899—1901. S. 1895-8. *Bldg. Com.* 1889-92. *Referee*, 1891-5. *Lib. Com.* 1885-87, 1892-5, 1898-9. *Ho. Com.* 1892-5, 1899—1901. *Trans.* 4.
- 1885 *PARKER, RUSHTON*, M.B., B.S., Professor of Surgery, University College, Liverpool (Victoria University); Surgeon to the Liverpool Royal Infirmary; 59, Rodney street, Liverpool.
- 1891 *PARKIN, ALFRED*, M.S., M.D., 24, Albion street, Hull. *Trans.* 1.
- 1879 *PEEL, ROBERT*, 120, Collins street East, Melbourne, Victoria.
- 1874 *PENHALL, JOHN THOMAS*, The Cedars, Broadwas-on-Teme, Worcester.
- 1897 *PERRAM, CHARLES HERBERT*, M.D., 55, Bromham Road, Bedford.
- 1879 *Pesikaka, HORMASJI DOSABHAI*, 43, Hornby road, Bombay.
- 1878 *Philpson, SIR GEORGE HARR*, M.D., D.C.L., Professor of Medicine in Durham University; Consulting Physician to the Newcastle-upon-Tyne Royal Infirmary; 7, Eldon square, Newcastle-upon-Tyne.
- 1898 *PHILLIPS, L. O. POWELL*, Kasr-el-Aini Hospital, Cairo.
- 1891 *PIERCE, BEDFORD*, M.D., The Retreat, York.
- 1897 *PIGG, T. STRANGEWAYS*, St. John's College, Cambridge.
- 1841 *Pitman, SIR HENRY ALFRED*, M.D., Consulting Physician to St. George's Hospital; Cranbrook, Bycullah park, Enfield. L. 1851-3. C. 1861-2. T. 1863-8. V.P. 1870-1. *Referee*, 1849-50. *Lib. Com.* 1847.
- 1892 *POWELL, HERBERT ANDREWS*, M.A., M.D., M.Ch., Piccards Rough, Guildford.

*Elected*

- 1900 *PRICE-JONES, CECIL*, M.B., 7, Claremont road, Surbiton, Surrey.
- 1897 *QUARTER-PAPAFIO, BENJAMIN WILLIAM*, M.D., Accra, Gold Coast, West Africa.
- 1857 *VON RANKE, HENRY*, M.D., 3, Sophienstrasse, Munich.
- 1890 *RANSOM, WILLIAM BRAMWELL*, M.D., Physician to the Nottingham General Hospital; The Pavement, Nottingham. *Trans.* 1.
- 1854 *RANSOM, WILLIAM HENRY*, M.D., F.R.S., Consulting Physician to the Nottingham General Hospital; 17, Park Valley, Nottingham. *Trans.* 1.
- 1902 *RAW, NATHAN*, M.D., B.S., 66, Rodney street, Liverpool.
- 1884 *REID, THOMAS WHITEHEAD*, M.D., Surgeon to the Kent and Canterbury Hospital; St. George's House, Canterbury, Kent.
- 1901 *REISSMANN, CHARLES HENRY*, M.D., B.C., B.Sc., St. Peter's, College Green, Adelaide, South Australia.
- 1881 *RICE, GEORGE*, M.B., C.M., Sutton, Surrey.
- 1889 *RIVERS, W. H. RIVERS*, M.D., St. John's College, Cambridge.
- 1871 *Roberts, DAVID LLOYD*, M.D., F.R.S.E., Consulting Obstetric Physician to the Manchester Royal Infirmary; Physician to St. Mary's Hospital, and Lecturer on Clinical Obstetrics and Gynæcology at the Owens College, Manchester; 11, St. John street, Manchester.
- 1889 *ROBERTS, LESLIE*, M.D., 46, Rodney street, Liverpool.
- 1873 *ROBERTSON, WILLIAM HENRY*, M.D., Consulting Physician to the Buxton Bath Charity and Devonshire Hospital; Buxton, Derbyshire.
- 1888 *Robinson, FREDERICK WILLIAM*, M.D., C.M., Huddersfield.
- 1885 *ROCKWOOD, WILLIAM GABRIEL*, M.D., Colombo, Ceylon.
- 1898 *Rogers, LEONARD*, I.M.S. [care of Messrs. Watson & Co., Calcutta.] *Trans.* 3.

*Elected*

- 1863 *ROWE, THOMAS SMITH*, M.D., Consulting Surgeon to the Royal Sea-Bathing Infirmary; Union crescent, Margate, Kent.
- 1891 *RUFFER, MARC ARMAND*, M.D., The Quarantine Board, Alexandria.
- 1865 *Sanderson, SIR JOHN BURDON, BART.*, M.D., LL.D., D.C.L.Durham, D.Sc., F.R.S., Regius Professor of Medicine in the University of Oxford; 64, Banbury road, Oxford. C. 1869-70. V.P. 1882. *Referee*, 1867-8, 1876-81. *Sci. Com.* 1862, 1870. *Lib. Com.* 1876-81. *Trans.* 2.
- 1867 *SANDFORD, FOLLIOTT JAMES*, M.D., V.D., late Surgeon-Major, 2nd Batt. S.V.L.Infy., now Hon. Surgeon-Major; Surgeon to the Market Drayton Dispensary, and Consulting Physician to the Market Drayton Cottage Hospital; Market Drayton, Shropshire.
- 1886 *SAUNDBY, ROBERT*, M.D., LL.D., Physician to the General Hospital, and Consulting Physician to the Hospital for Women, and to the Eye Hospital, Birmingham; Professor of Medicine, Mason University College; 140B, Great Charles street, Birmingham.
- 1883 *SCHAFER, EDWARD ALBERT*, LL.D., F.R.S., Professor of Physiology in the University of Edinburgh. C. 1899-1900. *Referee*, 1888-99. *Sci. Com.* 1889—.
- 1861 *Scott, WILLIAM*, M.D., Senior Physician to the Huddersfield Infirmary; Waverley House, Huddersfield.
- 1897 *SEMPLE, EDWARD*, M.D., Grove house, Fenstanton, Hunts.
- 1899 *SHUTTLEWORTH, GEORGE EDWARD*, M.D., Ancaster House, Richmond Hill.
- 1887 *SIDEBOTHAM, EDWARD JOHN*, M.B., Erlesdene, Bowdon, Cheshire.

*Elected*

- 1857 *SIORDET, JAMES LEWIS*, M.B., Villa Cabrolles, Mentone, Alpes Maritimes, France.
- 1896 *SLOANE, JOHN STRETTON*, M.B., B.S., B.Sc., 7, Highfield street, Leicester.
- 1891 *SMITH, G. COCKBURN*, M.D., 14, South road, Newton Abbot.
- 1902 *SMITH, HARRY LYON*, Woodfield House, Uppingham, Rutland.
- 1886 *SMITH, HOWARD LYON*, Buckland House, Buckland Newton, Dorchester.
- 1894 *SMITH, ROBERT SHINGLETON*, M.D., B.Sc., Deepholm, Clifton Park, Clifton, Bristol.
- 1894 *SMITH, THOMAS RUDOLPH*, M.B., B.C., Blythelholm, Stockton-on-Tees.
- 1868 *SOLLY, SAMUEL EDWIN*, Colorado Springs, Colorado, U.S.A.
- 1899 *STEPHEN, GUY NEVILLE*, Foreign Office Medical Staff.
- 1891 *STEVENS, SURG.-CAPT. CECIL ROBERT*, M.B., B.S., I.M.S., Eden Hospital, Calcutta.
- 1854 *STEVENS, HENRY*, M.D., late Inspector, Medical Department, Local Government Board, Whitehall; Durham Lodge, St. Margaret's road, Twickenham.
- 1884 *STEWART, EDWARD*, M.D., Brook House, East Grinstead.
- 1879 *Stirling, EDWARD CHARLES*, M.D., Senior Surgeon to the Adelaide Hospital; Lecturer on Physiology in the University of Adelaide, South Australia [care of Messrs. Elder and Co., 7, St. Helen's place].
- 1871 *STRONG, HENRY JOHN*, M.D., J.P., Consulting Surgeon to the Croydon General Hospital; Colonnade House, The Steyne, Worthing.
- 1890 *Symson, E. MANSEL*, M.D., B.C., Surgeon to the Lincoln County Hospital; Deloraine Court, Lincoln.
- 1886 *TEALE, THOMAS PRIDGIN*, M.B., F.R.S., Consulting Surgeon to the Leeds General Infirmary; 38, Cookridge street, Leeds.

*Elected*

- 1898 *THOMAS, J. LYNN*, C.B., Surgeon to the Cardiff Infirmary ; Consulting Surgeon to the Hamadryad Hospital ; Green Lawn, Pen-y-lan, Cardiff.
- 1890 *THOMAS, WILLIAM ROBERT*, M.D., Little Forest, Bath road, Bournemouth.
- 1891 *THOMSON, JOHN ROBERTS*, M.D., Monkchester, Bournemouth.
- 1876 *THORNTON, J. KNOWSLEY*, M.B., C.M., Consulting Surgeon to the Samaritan Free Hospital for Women and Children ; Hildersham Hall, Cambridge. C. 1891. *Lib. Com.* 1886-90, 1893-95. *Trans.* 5.
- 1883 *THUESFIELD, THOMAS WILLIAM*, M.D., Physician to the Warneford and South Warwickshire General Hospital ; Selwood, Beauchamp square, Leamington.
- 1880 *TIVY, WILLIAM JAMES*, 8, Lansdowne place, Clifton, Bristol.
- 1871 *Trend, THEOPHILUS W.*, M.D., 1, Grosvenor square, Southampton.
- 1881 *Treves, WILLIAM KNIGHT*, Surgeon to the National Hospital for Scrofula ; 31, Dalby square, Cliftonville, Margate.
- 1867 *TROTTER, JOHN WILLIAM*, formerly Surgeon-Major, Coldstream Guards ; 4, St. Peter's terrace, York.
- 1873 *TURNER, GEORGE BROWN*, M.D., Camden House, Hemel Hempsted, Herts.
- 1894 *TURNER, PHILIP DYMCK*, M.D., Sudbury, Isle of Wight.
- 1891 *TWEED, REGINALD*, M.D., Hembury Fort Cross, Honiton, Devon.
- 1881 *TYSON, WILLIAM JOSEPH*, M.D., Senior Medical Officer of the Victoria Hospital, Folkestone ; 10, Langhorne Gardens, Folkestone.
- 1900 *UHTHOFF, JOHN CALDWELL*, M.D., Wavertree House, Hove, Brighton.

*Elected*

- 1867 **VINTRAS, ACHILLE, M.D.**, late Physician to the French Embassy and Senior Physician to the French Hospital and Dispensary, Shaftesbury avenue; De Courcel road, Brighton.
- 1854 **WADDINGTON, EDWARD**, Hamilton, Auckland, New Zealand.
- 1868 **Walker, ROBERT**, Clovelly, Bideford.
- 1867 **WALLIS, GEORGE**, Consulting Surgeon to Addenbrooke's Hospital; 6, Hills road, Cambridge.
- 1899 **WALTERS, FREDERICK RUFENACHT, M.D.**, Crooksbury Sanatorium, Farnham, Surrey.
- 1883 **Walters, JAMES HOPKINS**, Surgeon to the Royal Berkshire Hospital; 15, Friar street, Reading.
- 1899 **WARDE, WILFRED BROUGHAM, M.D.**, 13, Lonsdale Gardens, Tunbridge Wells.
- 1861 **WATERS, A. T. HOUGHTON, M.D.**, Consulting Physician to the Royal Infirmary; 69, Bedford street, Liverpool. *Trans.* 3.
- 1874 **WELLS, HARRY, M.D.**, San Ysidro, Buenos Ayres, S. America.
- 1882 **WHARRY, CHARLES JOHN, M.D.**, 14, Ewell road, Surbiton, Surrey.
- 1881 **Whitehead, WALTER, F.R.S. Ed.**, Senior Surgeon to the Manchester Royal Infirmary, Manchester and Salford Lock Hospital, and Manchester and Salford Skin Hospital; Professor of Clinical Surgery, Owens College, Victoria University; 499, Oxford road, Manchester. *Trans.* 1.
- 1885 **Whittle, SIR WILLIAM, M.A., M.D.**, Professor of Materia Medica and Therapeutics, Queen's College, Belfast; Physician to, and Lecturer in Medicine at, the Belfast Royal Hospital; Consulting Physician to the Ulster Hospital for Women and Children; Consulting Physician to the Belfast Ophthalmic Hospital; 8, College square north, Belfast.

*Elected*

- 1870 *Wilkin, JOHN F.*, M.D., Rose Ash Court, South Molton, Devon.
- 1883 *Willans, WILLIAM BLUNDELL*, Much Hadham, Herts.
- 1896 *WILLIAMS, ALFRED HENRY*, M.D., Rotorua, Harrow.
- 1859 *Williams, CHARLES*, Senior Surgeon to the Norfolk and Norwich Hospital; 48, Prince of Wales road, Norwich.
- 1872 *Williams, Sir John*, Bart., K.C.V.O., M.D., Physician-Accoucheur to H.R.H. the Princess of Wales, Physician to H.R.H. the Princess Beatrice; Emeritus Professor of Obstetric Medicine, University College, London; Consulting Obstetric Physician to University College Hospital; Plâs Llanstephan, Carmarthenshire. C. 1891. *Referee*, 1878-90. *Lib. Com.* 1876-82.
- 1887 *WILSON, ARTHUR HERVEY*, M.D., 504, Broadway, Boston, U.S.A.
- 1889 *Wise, A. TUCKER*, M.D., Montreux, Switzerland.
- 1850 *Wise, ROBERT STANTON*, M.D., Consulting Physician to the Southam Eye and Ear Infirmary; Beech Lawn, Banbury.
- 1885 *WOLFENDEN, RICHARD NORRIS*, M.D., Rangemont, Seaford, Sussex.
- 1892 *WOODHEAD, GERMAN SIMS*, M.D., Professor of Pathology in the University of Cambridge; 6, Scrope terrace, Cambridge.
- 1879 *WOODWARD, G. P. M.*, M.D., Deputy Surgeon-General; 157, Liverpool street, Hyde Park, Sydney, New South Wales.
- 1899 *WINTER, ANDREW ELLIS*, M.D., Corner House, Beckenham, Kent.

*Corrected to 31st July, 1903.*



## ANNUAL GENERAL MEETING,

*March 2nd, 1903, at 5 p.m.*

---

*Present* :—ALFRED WILLETT, President.

G. NEWTON PITT, M.D., }  
CLINTON T. DENT, } Hon. Secs.,

and 26 Fellows.

The President nominated Dr. Whiting and Mr. F. Durham as Scrutineers, and declared the Ballot open until six o'clock.

Mr. Clinton Dent (Hon. Secretary) read the Report of the Council.

### REPORT OF THE COUNCIL.

The Council feel justified in congratulating the Society both on the present position of its affairs, and on the evidence of steady progress made during the last twelve months.

The numerical strength of the Society is quite up to the average, although an exceptionally large number of vacancies have been caused by death and resignation during the past year.

Since the last Annual Meeting 24 new Fellows have been elected, while the names of 33 Fellows have ceased to appear in the List, owing to death or resignation.

The following is a statement of the present numbers of Fellows :

Honorary Fellows—English	.	.	.	5	
Foreign	.	.	.	14	
				—	19
Fellows—Resident	.	.	.	524	
Non-resident	.	.	.	285	
				—	809
					—
Total	.	.	.	828	

The Council have great satisfaction in stating that all cause for anxiety with regard to the financial position of the Society in consequence of the termination of the lease of 53, Berners Street, may now be considered at an end.

The changes proposed by the Council and confirmed by the Society at the last Annual Meeting have been carried into effect, with results that exceed the anticipations that were formed.

The rooms formerly occupied by the Resident Librarian have now all been let on satisfactory terms, and bring in a net annual rental of £713. As a set-off against this increase of income a sum of £150 per annum paid to the Secretary as compensation, and a further sum of £20 per annum, being an increase in the salary of the Librarian, must be taken into account. The Council desires to remind the Society that the lease of 53 Berners Street premises falls in in December, 1904. This will involve a loss to the Society of £436 per annum; but with all deductions made it will be found that the new arrangement produces a substantial increase in the income of the Society.

A lift has been constructed to the second floor. The Council regret that the difficulties of carrying the lift to the third floor, as originally contemplated, were found to be insurmountable; but the addition as it now exists

undoubtedly increases the letting value of the upper rooms.

The following regulation as to the Secretary's attendance at the Society's Rooms has been included in the Standing Orders :

"The Secretary shall attend daily at the Society's house, his official hours being from 11 a.m. to 6 p.m., on Saturdays from 11 a.m. to 2 p.m. He shall be present in the Society's rooms from 11 a.m. to 12 noon and from 4 p.m. to 6 p.m., during which latter hours he shall always be accessible to the Fellows."

The Council have to report that a late highly esteemed Fellow—Mr. E. U. Berry—has bequeathed to the Society the sum of £300, free of legacy duty. This is not the only benefaction from Mr. Berry to the Society. Indeed, he was the first to make a gift to the Society at the time of the move from Berners Street to the present premises, and in the Report for 1890 the Building Committee acknowledged the sum of £124 which they had received from him as a contribution towards the Building Fund. Mr. Berry had been a Fellow of the Society since 1845. The Council desire gratefully to record this proof of the lasting interest that Mr. Berry took in the welfare of the Society.

The new method of dealing with papers read at the Society's meetings continues to work well, while the high quality of the papers contributed has been fully maintained.

The average attendance at the meetings has been sustained. The interest of the meetings has been largely added to by the acquisition of an epidiascope—the generous gift of an anonymous donor. The Council believe that the full value of the epidiascope for the illustration of papers has not yet been fully recognised by the Fellows, but they trust that in future the advantages of the instrument for demonstrating in the clearest possible manner every kind of object will be fully utilised.

The time has again come round for awarding the Marshall Hall Prize, under the terms of the Marshall Hall Memorial Trust. On the recommendation of the Special Committee appointed to consider the award, the Council propose that the prize, together with the diploma, be presented to Dr. Henry Head, and that he be requested to take an early opportunity of submitting to the Society a communication upon his recent work on the functions of the afferent nervous system.

The Committee appointed to investigate the subject of Suspended Animation in the Drowned have recently arrived at some highly important results. Their report will, it is hoped, shortly be submitted to the Fellows of the Society at a Special Meeting, and the Council feel it unnecessary therefore at present to anticipate in any way the report.

*Report of the Honorary Treasurers.*

"In presenting the balance-sheet to the Society the Honorary Treasurers wish to point out the heavy expenditure which has been caused by the structural alterations made in the Society's premises for the accommodation of the fresh tenants the Society has obtained for the upper floors, expenditure which might have been charged to the capital account. Owing to the volume of 'Transactions' for 1901 not being published until 1902 a portion of the payment for the volume for 1901 comes into the past year's account, and raises the expenses under that heading to the large sum of £601. The cost for the volume for 1902 was £354.

"The Library expenses also appear higher, which arises from the whole cost for the books purchased being debited to the Library account, instead of one half as has been heretofore the custom.

"The increase under '*Rent, rates and taxes, and*

*insurance*' is mainly due to the premium for our Septennial Fire Insurance Policy having been paid in the past year.

"Salaries and wages show some increase, which arises from the changes necessitated in the house staff of the Society, due to the lift and arrangements for the Society's tenants.

"On the receipt side the annual subscriptions exceed those of 1901 by £16 16*s.*, but the entrance fees are less by £59 17*s.* The Society's rental has been substantially increased, although only one quarter's rent has been as yet received from the new tenants.

"The statement of liabilities and assets shows that the financial position of the Society is in a thoroughly satisfactory condition."

*Report of the Honorary Librarians.*

"The Hon. Librarians are pleased to be able to report steady progress in the work of the Library.

"The total number of books added during the past year is 459,—294 of these by purchase and the remainder by gifts from Fellows and others.

"The issues (apart from books used in the Library) were 4189, an increase of some hundreds over previous years.

"Three hundred and thirty-one volumes have been borrowed from Lewis's library, as against 258 in 1901.

"A bookstore has been fitted up in the basement capable of shelving some 4000 volumes."

Sir William Church (Hon. Treasurer) explained the accounts.

The President moved—

"That the Report of the Council, together with the Treasurers' Statement of Accounts, be adopted."

Carried unanimously.

The President then called upon Dr. Henry Head, and said :

“Dr. Henry Head, it is now my most pleasing duty to inform you that this Society has acclaimed you its Marshall Hall prizeman for 1903.

“In the first place this prize was founded to perpetuate the memory of a very highly gifted scientist, and in the second for the encouragement of original research on lines of investigation to which the late Dr. Marshall Hall had consecrated his life's work. Instituted in 1872, the first award of it was made to Dr. Hughlings Jackson, in 1878. In successive quinquennia this prize has been bestowed on Dr. Ferrier, Dr. Gaskell, Sir William Gowers, and Dr. Sherrington.

“To you it cannot fail to be a source of most legitimate pride and gratification to find that—all unconsciously to yourself—you are now singled out, after a most thorough inquiry by a committee, as the man whose work in the past five years is adjudged to be pre-eminent for its originality, its completeness, and I venture to add for its promise of affording relief to suffering humanity, and that thereby your name is now linked for all time with those distinguished workers I have mentioned.

“Dr. Head, in now handing you this certificate declaratory of the award, and with it this cheque for £81 9s. 8d., being the amount of accrued dividends of the Trust Fund, it only remains for me to offer you in the name of the Society our heartiest congratulations, and to express to you the wish of the Society that you will favour us at one of our meetings with a communication upon your recent investigations in neurology.”

Dr. Head then briefly thanked the Society for awarding him the prize, and promised that he would at an early date make a communication on the subject of his researches.

The President then read the Annual Address (see p. ci).

Dr. Pavy moved, and Sir Felix Semon seconded—

“That the best thanks of the Society be given to the President for his address, and that he be, and is hereby requested to allow it to be printed in the ‘Transactions.’”

Carried unanimously.

Mr. Heath moved, and Mr. Page seconded—

“That the thanks of the Society be given to the retiring members of Council for their services to the Society during their respective terms of office—Dr. J. Kingston Fowler, Dr. de Havilland Hall, Sir Isambard Owen, Mr. Jacobson, Mr. Juler, Mr. Keetley, Mr. Lockwood, and Mr. Read.”

Carried unanimously.

At six o'clock the President called upon the Scrutineers to close the ballot. The Hon. Secretary announced that the following gentlemen had been duly elected as Officers and Council for the ensuing year :

*President.*—Alfred Willett.

*Vice-Presidents.*—Sir Richard Douglas Powell, Bart., M.D., K.C.V.O. ; Sir Dyce Duckworth, M.D., LL.D. ; N. Charles Macnamara ; Edgcombe Venning.

*Honorary Treasurers.*—Sir William Selby Church, Bart., M.D., K.C.B. ; J. Warrington Haward.

*Honorary Secretaries.*—George Newton Pitt, M.D. ; Clinton Thomas Dent.

*Honorary Librarians.*—Norman Moore, M.D.; Rickman J. Godlee, M.S.

*Members of Council.*—Henry Radcliffe Crocker, M.D.; Archibald Edward Garrod, M.D.; James Frederick Goodhart, M.D.; Wilmot Parker Herringham, M.D.; Amand Jules McConnell Routh, M.D.; A. Boyce Barrow; Anthony Alfred Bowlby, C.M.G.; Robert Marcus Gunn; George Robertson Turner; Edmund Johnson Spitta.



**(A) INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDING 31ST DECEMBER, 1902.**

Expenditure		£	s.	d.	£	s.	d.	Income	
Rent, Rates, Taxes, and Insurance ...	282	0	6		445	Annual Subscriptions at £3 8s.	1401	15	0
Salaries of Staff and Accountant ...	680	2	6		100	do.	£1 1s.	105	0
House Servants, Cleaners, etc.	242	10	6						
Lighting, Warming, and Cleaning ...	243	15	5			Composition Fees	...	1506	15
Printing and Stationery, Stamps and Telegrams ...	191	15	1			Entrance Fees	...	123	18
Meeting Expenses ...	39	1	6			Rents Receivable	...	126	0
Miscellaneous Disbursements ...	104	17	5			Sale of 'Transactions' ...	...	2696	4
						Interest on New South Wales Stock...	...	53	5
Alterations, Repairs, etc.				1794	2	11		12	6
Depreciation of Fixtures, Fittings, etc.				325	9	4		2	16
Library Purchases and Expenses ...				55	8	5			
Interest on Debentures ...				484	2	0			
				1023	12	9			
Scientific Committees ...				12	0	6			
'Transactions' ...				601	0	0			
'Climates and Baths' ...				43	6	9			
Audit Fee ...				10	10	0			
Balance, being excess of Income over Expenditure during the year ...				191	12	10			
				£4521	5	6			

Income  
 Consols on Dec. 31st, 1901  
 Dividends for 1902

Excess of Income over Expenditure for the year 1901-1902

228,110 16 2

228,110 16 2

# MARSHALL HALL FUND.

Consols on Dec. 31st, 1901  
 Dividends for 1902

## PERMANENT ENDOWMENT FUND.

New South Wales 4 per cent. Inscribed Stock, 31st December, 1901, £200 10s. 10d.

10th February, 1903.

W. S. CHURCH,  
 WARRINGTON HAWARD, } Hon. Treasurers.

Audited and approved,  
 J. G. MUNDY, F.C.A.

10th February, 1903.

Income

Consols on Dec. 31st, 1901

Dividends for 1902

Excess of Income over Expenditure for the year 1901-1902

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## LIST OF PAPERS.

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N.B.—The Council of the Royal Medical and Chirurgical Society deem it proper to state that the Society does not hold itself in any way responsible for the statements, reasonings, or opinions set forth in the various papers which, on grounds of general merit, are thought worthy of being published in the *Transactions*.

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I. A Note on the Causation and Treatment of Thrombosis occurring in connection with Typhoid Fever; by ALMROTH E. WRIGHT, M.D., Pathologist to St. Mary's Hospital; late Professor of Pathology, Army Medical School, Netley; and H. H. G. KNAPP, M.D., Lieut. Indian Medical Service . . .	1
II. On Acute Cerebro-spinal Meningitis caused by the <i>Diplococcus intracellularis</i> of Weichselbaum: a Clinical Study; by CECIL WALL, M.A., M.D.Oxon., M.R.C.P. (Communicated by FRANCIS WARNER, M.D., F.R.C.P.) . . .	21
III. The Clinical Associations of Reduplicated First Sounds, based on a Series of One Hundred and Nine Cases; by ARTHUR G. PHEAR, M.D. . .	129
IV. The Clinical History and Symptoms of One Hundred and Twenty Cases of Exophthalmic Goitre; by GEORGE R. MURRAY, M.A., M.D.Camb., F.R.C.P., Heath Professor of Comparative Pathology in Durham University; Physician to the Royal Infirmary, Newcastle; President of the Northumberland and Durham Medical Society. (Communicated by Sir THOMAS BARLOW, Bart., M.D.) . . .	141
V. Paroxysmal Hæmoglobinuria of Traumatic Origin; by C. W. ENSOR, M.R.C.S.Eng., L.R.C.P.Lond., and J. O. W. BARRATT, M.D., B.Sc.Lond., F.R.C.S.Eng. (Communicated by Dr. VAUGHAN HARLEY) . . .	165

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VI. The Differentiation of the Continued and Remittent Fevers of the Tropics by the Blood Changes; by LEONARD ROGERS, M.D., M.R.C.P., I.M.S., lately Acting Professor of Pathology, Medical College, Calcutta . . . . .	197
VII. Latent Empyema in Infants; by S. VERE PEARSON, M.B.Cantab., M.R.C.P.Lond., Assistant Physician to the East London Hospital for Children, Shadwell; Medical Registrar to St. George's Hospital. (Communicated by Dr. ROLLESTON) . . . . .	235
VIII. A Statistical Inquiry into the Prognosis and Curability of Epilepsy, based upon the results of treatment; by WILLIAM ALDREN TURNER, M.D., F.R.C.P., Physician to Out-patients, the National Hospital for the Paralysed and Epileptic, Queen Square; and to King's College Hospital . . . . .	259
IX. A Further Report on the Remarkable Series of Cases of Molluscum Fibrosum in Children communicated to the Society by Dr. John Murray in 1873; by ARTHUR WHITFIELD, M.D., M.R.C.P., and ARTHUR H. ROBINSON, M.D., M.R.C.S., D.P.H. . . . .	293
X. A Report on Four Cases of Acute Septic Inflammation of the Throat, with Bacteriological Examination of each: a Sequel to a similar Paper read by Sir Felix Semon, April, 1895; by PHILIP R. W. DE SANTI, F.R.C.S., Surgeon to the Throat, Nose, and Ear Departments at Westminster Hospital . . . . .	303
XI. Rise of Blood-pressure in Later Life; by Professor T. CLIFFORD ALLBUTT, F.R.S. . . . .	323
XII. Supra-pubic Cystotomy in Cases of Tumour of the Bladder, with Special Reference to the Causes of Mortality and of Recurrence of the Growth; by CHARLES BARRETT LOCKWOOD, F.R.C.S., Assistant Surgeon to St. Bartholomew's Hospital . . . . .	345
XIII. A Case of Aneurysm of the Abdominal Aorta treated by the Introduction of Silver Wire; with a Description of Instruments invented and constructed by Mr. G. H. Colt to facilitate the introduction of Wire into Aneurysms; by D'ARCY POWER, M.A., M.B., and G. H. COLT, B.A. . . . .	363

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ADDRESS  
OF  
ALFRED WILLETT

PRESIDENT

AT THE

ANNUAL MEETING, MARCH 2ND, 1903

---

A.D. 1902 will be ever memorable in the history of this country for the pathetic incidents attaching to the sudden illness of our gracious patron King Edward VII, on the very eve of the date, June 26th, which had been many months previously appointed for His Majesty's and Queen Alexandra's Coronation.

Happily now it is but history that under the merciful dispensation of Providence the source of grave danger to His Majesty's life was removed. In this assembly it is but fitting to mention that this fortunate result was due to the prudent, yet firmly tendered advice of His Majesty's responsible medical advisers, and before all to the skill of Sir Frederick Treves, upon whom fell the duty of performing the operation for a critical condition of suppurative appendicitis. So again, it is but history to relate how rapidly and completely the King convalesced,

and how on August 9th, only six weeks and two days later than the originally appointed day, the deferred ceremony of the Coronation of their Majesties was duly solemnised in Westminster Abbey, King Edward being at that time restored to perfect health.

The useful and important work of this Society has followed the even tenor of its way, undistracted by any of the exciting incidents of an eventful year.

Whilst the attendance of Fellows at our ordinary meetings has been up to the average and the contributions ample, many, indeed, being of exceptional value and interest, nevertheless I, as several of my predecessors have done in past years, feel it incumbent to state that this fine meeting-room is as a rule very inadequately filled, having in view the number of Fellows on the roll.

The epidiascope—which the Society now possesses through the munificent generosity of an anonymous donor, generosity the more notable because he is unconnected with the Society—cannot fail to be of very material assistance to authors in illustrating their papers, and this probably in more ways than are yet realised.

The Council's report has told you of the large rental obtained from letting the rooms on the two floors, formerly the residence of Mr. MacAlister, and which enables the Society to view the surrender of the Berners Street lease without the slightest apprehension of financial straits. The successful letting has been without doubt greatly facilitated by the installation of a hydraulic lift to the second floor.

The Treasurer's report is satisfactory. It does not call for comment here.

The publication in the course of the year of vol. ii of 'Climates and Baths of the United Kingdom' completes the report of the Spas Committee. I venture to invite Fellows to acquire this important work issued by the Society.

In 1905 the Royal Medical and Chirurgical Society will have existed for 100 years. It will be, I feel sure, the



wish of the Fellows that at our next Annual Meeting the Council should submit proposals for commemorating the Society's Centenary in a way befitting this event.

The Marshall Hall prize having been presented to Dr. Head at an earlier stage of to-day's proceedings, I will now proceed to speak of the losses the Society has sustained by death, for a reference to each of the colleagues that have passed away finds a time-honoured place in the President's annual address.

Death has in the past year, I deeply regret to state, robbed the Society of an unusually large number of its Fellows. No less than 24 have been in this way taken from our roll-call, and of these 13 were Resident, 8 Non-resident, 1 Honorary, and 2 Foreign Honorary Fellows; but it is to be noted that, with few exceptions, longevity had been attained, 14 having passed the Scriptural allotted span of threescore years and ten.

I would take this opportunity of gratefully acknowledging my indebtedness to Fellows who have kindly helped me in the compilation of the following obituary memoirs.

*Dr. Edwin Matthews James*, who for some thirty years held a leading position as a surgeon at Melbourne, Victoria, died on July 6th, 1900, at The Pavilion, Melrose, N.B., at the age of 71.

Elected a Fellow of this Society in 1892 upon his return to England after his retirement from the practice of his profession in Australia, Dr. James did not contribute to our 'Transactions,' nor did he hold office; nevertheless, whilst in Australia he was for many years a member of the Medical Society of Victoria, and was elected its President in 1883.

Edwin Matthews James, a son of the Rev. W. J. James, Rector of Clive, Salop, was born in 1829. Educated privately, he was, whilst in his teens, apprenticed to Dr. J. N. Heathcote of that town, and in 1850 became a resident pupil of the Salop Infirmary. In this way he

acquired an insight of medical and surgical practice which was to be of much advantage to him. Owing to the "*res angusta domi*," and attracted, as so many were, by visions of quickly acquired wealth, on the news of the discovery of gold in Australia, James, in company with some of his acquaintances, started in May, 1853, for the "Diggings." He appears to have met with but qualified success, for after experiencing the vicissitudes and caprices of this adventurous life he turned his footsteps towards Melbourne, where, at the recently started hospital, he obtained the position of Dispenser, and later was made Assistant House Surgeon. Realising, however, the necessity of becoming a legally qualified surgeon, he returned to England, and on October 1st, 1858, entered as a student at St. Bartholomew's Hospital. His chief companion during this period was the late William Morant Baker, with whom, indeed, as with many other friends of his student days, he kept up a lifelong intimacy.

Whilst a student at St. Bartholomew's, James devoted himself with much keenness to the study of anatomy, and there is in existence a minor instrument case, of the possession of which he was justly proud. It bears this inscription, "Presented by Edward Stanley, F.R.S., Surgeon to St. Bartholomew's Hospital, to Mr. Edwin James, for his great proficiency in anatomical knowledge, 1859."

It is interesting to mention here that during his absence from Melbourne his position as Assistant House Surgeon at the hospital was temporarily filled by the present Sir T. N. Fitzgerald.

James qualified in 1860, after only two years' attendance at a London medical school. This he had been enabled to do by virtue of his former residence at the Salop Infirmary, which enabled him to count the time spent there as part of the regulation period of three years' hospital practice for the Hall and College diplomas. He at once returned to Melbourne and resumed his position of Assistant House Surgeon at the hospital. He became

Senior Resident in 1864. Not long after, viz. in 1865, he was elected Surgeon, and was soon hard at work in practice. He was universally esteemed. High and low, rich and poor, were attracted by his fame as a surgeon, whilst his ability, skill, and sterling good qualities made all his patients his friends.

There is but little doubt that for many years Mr. James's practice was one of the largest and most lucrative that any member of the profession has ever enjoyed in Melbourne. In 1884, being at that time Medical Adviser at Government House, he accompanied the retiring Governor, the Marquis of Normanby, on his return to England, and was absent from the Colony for about eighteen months.

In 1869 Mr. James married a daughter of Mr. John Matheson, General Manager of the Bank of Victoria, who had gone out from England as a lad to join relatives and to make his way, and who had gradually risen to that responsible position.

James gave energetic support to every movement for the development and material prosperity of his adopted country. He was particularly keen on all kinds of sport; he imported greyhounds and ran them in coursing events for many years, but fishing was his especial passion. His holidays were always spent in Tasmania, where it is believed he was the first to take a trout of great size from imported ova; it weighed 18 lbs., and its capture was noticed in the 'Field.'

Having accumulated a considerable fortune, and after thirty years of professional life, James left Melbourne to spend the closing years of his life in this country. He had a house in London, but his chief resort was the banks of the Tweed at Melrose, N.B. He rented the Pavilion Water for many years, engaging in his favourite sport of fishing, and here, after an illness of more than two years from cancer of the breast, he died. At his express wish his remains were interred in the General Cemetery at Shrewsbury.

A most genial, warm-hearted man, James was universally popular, and loved by all who enjoyed his friendship.

Mrs. James and two daughters survive him.

*Dr. William Lewis Dudley* died at Cromwell Road, West Kensington, on March 7th, 1902, aged 81 years. The important part of his professional life was spent in Bogota, the capital of the Republic of Columbia, into which country it is said that he introduced the custom of vaccination. Dr. Dudley was elected a Fellow in 1876, but had not held office.

A Fellow of the Society, who is familiar with his career, has supplied the following details :

"He was my senior at St. Bartholomew's School of Medicine by at least four years. I knew him only by sight during 1845. In 1846 (or 1847) I knew more of him, for it was my father's lot to have the appointment of Medical Officer to a mine—St. Anna. Dudley was the candidate whom my father appointed. Whenever he came to England, as he did, I think, in 1859 or 1860, he came and saw us frequently. He then showed his energy and ability in taking his degree in Medicine as M.D. at St. Andrews and the Fellowship of the Royal College of Surgeons of England.

"I forget when he came back for good, but he had then made enough to retire from active practice.

"I found him—to satisfy his desire for professional work—the post of Physician to the City (of London) Dispensary, to which I was the Surgeon. He held this appointment almost to the last. I believe that he was occasionally consulted in the neighbourhood of his dwelling in South Kensington."

It is improbable that any of the circumstances of his professional life in Central America will ever come to light, but from the fact that he was Physician to both the English and American Legations it is fair presumption that he held a leading position as a medical practitioner.

In 1854 he wrote a 'Treatise on Cholera Morbus,' and, in 1862, 'Clinical Observations on Urethral Stricture.'

*Sir William Guyer Hunter*, K.C.M.G., M.D., Honorary Surgeon to Queen Victoria, Knight of Grace of the Order of St. John of Jerusalem, Surgeon-General (retired) of the Indian Army, Bombay Presidency, whose career in India was passed chiefly in Bombay, and who after his return to England was elected M.P. for Central Hackney, died at the age of 74, on March 14th, 1902, at his residence on Anerley Hill. Sir Guyer Hunter was elected a Fellow of this Society in 1873, but he never held any office in it, nor did he make any contribution to the Society's 'Transactions.'

Sir Guyer Hunter was the son of Thomas Hunter, of Catterick, North Riding of Yorkshire, and was born in Calcutta in 1827. Educated at King's College School, he entered as a medical student of Charing Cross Hospital in 1844, and became M.R.C.S. in 1849. He became F.R.C.S.Edin., 1858; M.D.Aber. and M.R.C.P.Lond., 1867; and was elected F.R.C.P.Lond., 1875.

Shortly after qualifying, Guyer Hunter was given an appointment as Assistant Surgeon in the Bombay Medical Service in May, 1850. He saw active service in the second Burmese campaign, during which his life was imperilled by an attack of cholera. In 1854 he received high commendation from the Bombay Medical Board for successfully establishing dispensaries in Raligaum, Alighur, and Shikarpur, and in 1857 the thanks of Government for zeal and skill during a fever epidemic in Shikarpur; also for suppressing a revolt of eight hundred prisoners in the jail of that station. He served with great distinction throughout the entire period of the Indian Mutiny, and received the thanks of Government and a medal.

After furlough in England Hunter returned to India to take up the appointment of Physician to the Jamsetjee Jeejeebhoy Hospital and Professor of Medicine in the Grant Medical College, of which he was made Principal

in 1876. This institution greatly prospered under his administration, the number of students increasing from sixteen to two hundred ; and to mark the importance of the work he had done for education he was in 1879 made Vice-Chancellor of the University of Bombay. In 1876 he had been made Deputy Surgeon-General, and in 1878 Surgeon-General, and received thanks from Government for organising the Medical and Hospital Equipment for active service when troops were sent to Malta from India, and his scheme was ultimately adopted throughout India.

In 1880, when Hunter retired from the Service, the Government issued a very complimentary Order, in which his services were greatly commended and his retirement regretted ; he was also recommended for a distinction, and received the appointment of Hon. Surgeon to the late Queen. The wide-spread regret felt at his departure was evidenced by the numerous farewell addresses presented to him. Soon afterwards his old school—Charing Cross Hospital—elected him a Consulting Physician. In 1883, on the occasion of a severe outbreak of epidemic cholera in Egypt, Hunter, at the request of the President of the Indian Medical Board, was appointed to investigate it. He wrote an able report, showing the urgent need of efficient sanitation in Egypt and emphasising the infinitely greater value of sanitary measures over quarantine regulations in arresting the spread of cholera. In this year, in recognition of his many important services, he was made K.C.M.G.

Sir Guyer Hunter took an active share in originating the formation of the Volunteer Medical Staff Corps in England, of which he was given the command. In 1885 he was elected M.P. for Central Hackney ; he was a most active and useful member, and commanded the attention of the House in all questions involving the public health ; he retired from Parliament in 1892. As a representative of Great Britain he attended in 1885 the Sanitary Conference at Rome, at which he was one of the

most prominent supporters of medical inspection in place of quarantine. From 1886 to 1887 he was a member of the School Board for London, Westminster Division. He was for many years a Vice-President of the Sanitary Institute, and worked hard for it up to the day of his death.

The whole career of a life which was terminated suddenly by an acute attack of disease was one of singular activity, energy, and professional ability. Hunter was held in the highest respect both privately and professionally, and his services, especially to medical education in Bombay, conduced greatly to the high position it now occupies. He was admired and regretted by all classes of the community, and few medical officers will hold a higher place in the memory alike of the Government and the people than William Guyer Hunter.

*Athol A. W. Johnstone*, F.R.C.S., the earlier part only of whose professional career was passed in London, as a member of the Teaching Staff of St. George's Hospital and as Surgeon to the Hospital for Sick Children in Great Ormond Street, died at the age of 81 on March 16th, 1902, at Brighton, to which town he had removed in 1862.

Athol Johnstone was elected a Fellow of this Society in 1848, and served on its Library Committee in 1860. He contributed a paper on "Rupture of the Liver and Spleen," published in vol. xxxiv of the 'Transactions.'

Mr. Athol Johnstone was born in 1820, and was the youngest son of Dr. James Johnson, Physician to King William IV, and who had settled in London after a long professional life abroad, and enjoyed a considerable reputation in the treatment of tropical disease. After his death his sons resumed their original family name of Johnstone.

Mr. Athol Johnstone was connected with the school of St. George's Hospital, as House Surgeon, Demonstrator of Anatomy, and as Lecturer on Physiology. No one was more popular or more efficient in all these capacities.

His charming manner, his unaffected wit, and his brilliant illustrations rendered his lectures a real pleasure to his hearers, and it was at his own choice to secure a place on the Staff of the Hospital. His surgical abilities were undoubted; he succeeded Mr. George Pollock as Surgeon to the Hospital for Sick Children in Great Ormond Street, and he was remarkable both for his judgment as a surgeon and his dexterity as an operator. It was, perhaps, especially in lithotomy that he gave proof of the latter quality. The care, neatness, and celerity with which he performed an operation, not always free from difficulty, in the narrow room of a child's perineum, were the constant theme of admiration to those who followed his practice.

Mr. Johnstone's contribution to our 'Transactions' was written with the object of demonstrating the possibility of recovery from traumatic rupture of the liver or spleen, founded on his own experience as House Surgeon at St. George's.

Mr. Athol Johnstone's brother, James, a man of brilliant talents and wide popularity, was for a few years Assistant Surgeon at St. George's Hospital; but he thought his health too uncertain to bear the strain of an operating surgeon's life, and he accordingly resigned his hospital appointment. Still he lived to a good old age, and one, at least, of the literary efforts of James Johnstone attracted much notice at the time, viz. the letters of "An Englishman," describing the *coup d'état* of December 2nd, 1848, of which he was an eye-witness.

Mr. Athol Johnstone had married early, but lost his wife not long afterwards. In 1861 he married the lady who now survives him, and shortly afterwards moved to Brighton, where he resided till his death. Just at that time the sudden death of Mr. Henry Gray, who was on the point of being elected, without opposition, as Assistant Surgeon at St. George's, made his former colleagues at that school sound Athol Johnstone as to the possibility of his standing for the vacancy. But he did not think him-



self physically strong enough to face the toils of life in London. He lived universally respected at Brighton, serving as Surgeon to the Children's Hospital there and enjoying as much practice as he chose to undertake. He occasionally diverted himself with anonymous *jeux d'esprit*—which were very successful, but which he never acknowledged,—and sometimes enjoyed a sea voyage. And so ended a long, happy, and prosperous, though very unambitious career, at over 80 years of age.

I am indebted to a former President of this Society for the foregoing interesting memoir of his old friend.

*Edward Long Fox*, M.D.Oxon., F.R.C.P., who for very many years held a leading position as a physician in the West of England, died on March 28th, 1902, at his residence, Church House, Clifton, in his 70th year.

Dr. Long Fox became a Non-resident Fellow of the Royal Medical and Chirurgical Society in 1859. He did not contribute to its 'Transactions.'

Edward Long Fox, the eldest son of Dr. Francis Kerr Fox, of Brislington, near Bristol, was born in 1832. At the age of 13 he went to Shrewsbury School, at which time Dr. Kennedy was Head Master. He was very active in all school games, and was "coxswain" of the school "eight." In 1850 he entered at Balliol College, Oxford, and had for his college tutor the celebrated Professor Jowett, and he was a pupil of Sir Henry Acland's at the Radcliffe Infirmary. He took his degree in 1853, obtaining a First in Natural Sciences, and shortly after paid a short visit to Edinburgh. In 1854 Long Fox became a student of St. George's Hospital, and was a clinical clerk to Dr. Bence Jones. During his student days he attended also the clinical practice at the Brompton Consumption Hospital, and at the Hospital for Sick Children, Great Ormond Street. He became M.B.Oxon. 1857, and M.D. 1861, M.R.C.P. 1859, and was elected to the Fellowship of the College in 1870, and to the Council in 1888. In 1857 he had been appointed Physician to the Bristol Royal Infirmary,

to which institution it is noteworthy that his grandfather had been Physician in 1786, and his uncle in 1816. Dr. Long Fox was Lecturer in Medicine and in Practical Pathology in the Bristol Medical School, and was at one time an Examiner in Medicine at Oxford. He delivered the Bradshaw Lecture at the College of Physicians in 1882. He was a past President of the Bristol Medico-Chirurgical Society and of the Bath and Bristol Branch of the British Medical Association, and was President of the parent Association at the Bristol Meeting in 1894.

One of our Fellows, who knew the late Dr. Long Fox well, has kindly supplied me with the following sketch of his career in the West of England :

Dr. Edward Long Fox, having taken a First Class in Natural Sciences at Oxford, was at a very early age elected Physician to the Royal Infirmary at Bristol. Such a post could then only be held for twenty years, so that he had passed through his active work as a Hospital Physician and had become a member of the Consulting Staff soon after he was 40. Following after Symonds and William Budd, and having as compeers Martin, Beddoe, Fripp, and Brittan, he was for many years looked upon as the leading physician in Clifton, if not in the West of England. His high character, handsome face, and courteous manner assisted in making him always acceptable, both in the sick room and at social gatherings, and he was one of the best known and most respected citizens of Bristol. He maintained a high standard of conduct in relations with his professional brethren, who felt proud of him not only on account of his medical ability, but because he was a thorough gentleman in all the best senses of the word, a man of culture and of refined and conscientious feeling—and he held a high place in their estimation as a reliable and helpful medical opinion.

He rapidly acquired a large and lucrative practice, which made such claims upon his time that he could find but little leisure for writing very full records of his wide experience.

Moreover had he been a stronger man he would probably have done more in what may be called the field of original work, but he was early affected by gout, which no doubt made it sometimes difficult for him to satisfactorily perform the severe routine of his practice.

Dr. Fox was a man of strong religious feeling, and he did his best to live up to the standard and doctrine of the Christian faith. He was very unselfish, considerate for the shortcomings or mistakes of others, and generous with his purse to many philanthropic objects, and particularly where he knew that a professional brother was in need.

Of a retiring disposition, he was disinclined to come prominently before the public, but he took a strong line in favour of establishing homes for the treatment of tuberculous patients, and he was an uncompromising advocate of total abstinence from alcohol and a prominent champion in the cause of temperance reform.

*Dr. Alexander MacGregor*, after practising in Aberdeen for some fifteen years, came to London in 1895, and died on April 12th, 1902, at his residence in Queen Street, Mayfair, at the age of 48.

Dr. MacGregor was elected a Fellow in 1896, but he did not contribute to our 'Transactions,' nor had he held office in the Society.

Alexander MacGregor, the son of a Highlander, was born in 1854 at Invergordon. He was educated at a private school, but received his medical education at the University of Aberdeen, where at the age of 24 he passed out as M.B., C.M., with highest honours, and he then spent some time at Vienna and Berlin. Settling in Aberdeen in 1880, he quickly rose to fame and had a large practice, whilst in the University he held successively the appointments of Demonstrator of Anatomy under Professor Struthers, and of Assistant to the Professor of Medical Jurisprudence, and subsequently Assistant to the Professor of Medicine; whilst in 1893 he was appointed

Rector's Assessor in the University Court for the Marquis of Huntly.

In 1895, being unsuccessful in his candidature for the Professorship of Medicine at the University, Dr. MacGregor determined to come to London, and settled in Harley Street, removing a few years later to Queen Street, Mayfair. He became M.R.C.P.Lond., and was appointed Physician to the North-west London Hospital for Diseases of the Chest, and to the Westminster Dispensary. When cut off in the prime of manhood by angina pectoris he had been established in London scarcely long enough to be as well or as widely known as he deserved; but at Aberdeen he will be long and affectionately remembered. Throughout life Dr. MacGregor was an ardent Volunteer, and for many years was Surgeon-Commandant of the Aberdeen Volunteer Medical Staff Corps, and after coming to London he joined the 19th Battalion of the Rifle Brigade.

Dr. MacGregor was a physician of sound judgment and strong good sense, kindly in nature, shrewd, and warm-hearted.

*William Tickle Whitmore*, who practised as a consulting surgeon in London, died on May 13th, 1902, at the age of 51, at Leamington, his premature death being due to arterio-vascular degenerative changes.

Mr. Whitmore was elected a Fellow of this Society in 1877. He did not contribute to our 'Transactions,' neither had he held any office.

The son of Mr. W. Whitmore, of Norris Street, Haymarket, he was born in 1850, and was partially educated in France. He commenced to study medicine at St. Bartholomew's Hospital in 1869. He qualified in 1874 by passing the M.R.C.S. examination. He was L.S.A. in 1875, and in 1877 he obtained the F.R.C.S.Edin.

Mr. Whitmore was for a year House Surgeon and Administrator of Anæsthetics at the West London Hospital. He then commenced practice in Arlington Street, where he resided for many years, until his health

gave way some eight years ago, when he retired to Brighton. He was one of the Founders of the Gordon Hospital for Fistula, and became one of its Surgeons.

He leaves a widow, the daughter of the late Dr. Allen, of Regency Square, Brighton, and one son.

For twenty years Whitmore was an energetic Volunteer, obtaining a commission in 1877 as Assistant Surgeon to the 3rd City of London Rifle Brigade. He rose to the rank of Surgeon Lieut.-Colonel, and received the "V.D." medal for long service. Whitmore also was an active Freemason, and ranked as P.M. and P.G.S. Moreover he was musical, and fond of shooting and other rural pursuits. As a young man he was an expert swimmer and diver, often exciting the envy of those who witnessed his aquatic performances.

William Tickle Whitmore—says one who knew him well—will be remembered by many as a staunch and sympathetic companion and friend; upright, conscientious, thoroughly kind-hearted, and considerate to the needs of others.

*Dr. William Miller Ord*, one of the best known and hardest working physicians in London, died on May 14th at The Hall, Salisbury—the residence of his son—in his 68th year.

Elected a Fellow in 1873, Dr. Ord served on the Council in 1889-90, on a Science Committee in the same year, and as a Referee 1884 to 1888. He made no less than six contributions to the Society's 'Transactions,' viz.:

"Case of Duchenne's pseudo-hypertrophic muscular paralysis."—'Med.-Chir. Trans.,' vol. lvii.

"Urinary crystals and calculi: Observations on the circumstances determining the forms of crystalline deposits in urine, and the production of renal and vesical calculi."—Vol. lviii, p. 165.

"Notes of a case of pseudo-hypertrophic paralysis, with observations on surface thermometry."—Vol. lx, p. 19.

"On myxœdema, a term proposed to be applied to an

essential condition in the cretinoid affection occasionally observed in middle-aged women.”—Vol. lxi, p. 57.

“Malformation of the genital organs of a man associated with persistence of one of the ducts of Müller.”—Vol. lxiii, p. 11.

(With Dr. Brodie Sewell) “Account of a large dermoid cyst found in the abdomen of a man.”—Vol. lxiii, p. 1.

William Miller Ord was born at Brixton Hill in 1834, and was the eldest son of Mr. George Ord, at that time a well-known and highly esteemed medical man in very extensive practice. Young Ord was educated at King's College School, but after matriculating at the University of London entered at St. Thomas's Hospital for his medical education about 1852. Ord's career at St. Thomas's as a medical student was distinguished; he gained numerous prizes, including the Cheselden Medal in Surgery. It would appear as if at this time his bent was towards surgery, for he held the appointments of House Surgeon and Surgical Registrar at his hospital; but then he joined his father, and thus the first few years of his professional life were spent in the busy routine of a large general practice, although for a part of the time he was lecturing on Comparative Anatomy at St. Thomas's.

In 1871, on the completion of the present hospital at Stangate, Dr. Ord was elected Assistant Physician, and in 1877 attained the position of full Physician, and shortly afterwards he became joint Lecturer on Medicine. He had been elected a Fellow of the Royal College of Physicians in 1875, and for many years was Dean of the Medical School. He resigned his lectureship in 1894, and retired from St. Thomas's in 1898, in accordance with regulation, after twenty years' service on the Senior Staff.

Both as a consultant and teacher Ord was highly esteemed and most successful. He read widely, had an extensive acquaintance with classic literature, ancient and modern, was ardently devoted to science, and was the possessor of a truly marvellous memory; but it is as a

teacher of clinical medicine that Ord will be chiefly remembered. Methodical in unravelling the points of a case, he was lucid in exposition, and with a witty, attractive manner he held the attention of his large class throughout his visit to the wards. One of his best characteristics was his habitual punctuality.

For many years Dr. Ord enjoyed a large consulting practice, and he was greatly endeared to his patients, whilst in all professional circles his genial manner and flow of spirited conversation made him ever a welcomed and attractive personality. For some time it had been apparent that Ord's health was failing, and some eighteen months before his end he retired into the country near to Andover, but, becoming seriously ill, he was removed to and died at his son's house.

Ord, considering the work he got through, was a prolific writer, his most notable productions being on *Myxœdema*, and for our present-day knowledge of this subject the profession owes more to him than to anyone else. His researches culminated in the Bradshaw Lecture at the College of Physicians in 1898 on "*Myxœdema and allied conditions.*" He also edited the '*Collected Works of Dr. Francis Sibson.*'

By the death of *Dr. John Wychenford Washbourn*, C.M.G., Physician to Guy's Hospital, in the prime of life, the profession loses one who had already achieved fame, for his name will always be associated very prominently with the pathology of pneumonia. He died at Tunbridge Wells on June 20th, 1902, in his thirty-ninth year, of acute tuberculosis following influenza and pleurisy.

Dr. Washbourn was elected a Fellow in 1889, and contributed a paper to the Society's '*Transactions*' in 1894 on "*Three Cases of Pleurisy caused by the Pneumococcus.*"

Dr. John Wychenford Washbourn, the second son of the late Mr. W. Washbourn, of Gloucester, was descended from the Washbourns of Washbourn and Wychenford, in

the county of Worcestershire. He was born on June 22nd, 1863, and was educated at King's College, Gloucester.

In 1880 he obtained the Entrance Scholarship in Science at Guy's Hospital, and carried everything before him during his career at the hospital. He threw himself heart and soul into everything he did, whether it was his work or his amusement.

Among other prizes at Guy's Hospital he took the Treasurer's Gold Medals in Surgery and in Medicine; and at the London University the Exhibition and Gold Medal in Organic Chemistry at the first M.B., the Scholarship and Medal in Medicine, and the Medal in Forensic Medicine. In 1887 he qualified for the Gold Medal at the M.D. examination. He took the F.R.C.S., and was elected a Fellow of the Royal College of Physicians of London in 1894. After qualifying, he spent a year abroad studying bacteriology under Professor Grüber in Vienna, with Professor von Baumgarten in Königsberg, and later on with Professor Celli at Rome. In 1888 he was appointed Demonstrator of Anatomy in the Guy's Hospital Medical School, and in 1890 Assistant Physician. He now organised and equipped the Department of Bacteriology, which he brought into a state of great efficiency. A few years later he was appointed Lecturer on Physiology, and soon after on Bacteriology. In 1889 he was elected Assistant Physician, and in 1892 Physician to the London Fever Hospital. He became much interested in this work, and with his friend, Dr. Goodall, he brought out their well-known manual on 'Infectious Diseases,' founded on the extensive experience he had thus obtained.

In April, 1893, he married Miss Florence Carr, of Greenwich, but his happy married life was cut short by her death a few days after the birth of their first child. His daughter survives him.

He was a fellow or member of several medical societies, and at the time of his death was Honorary Secretary of the Epidemiological Society and of the British Medical Association.



The subject in which he was most interested, and in connection with which his name was best known both here and abroad, was the lesions associated with Fraenkel's pneumococcus and the preparation of antipneumococcic serum. He had worked at the subject from many points of view for the past ten years, both alone and in connection with his friend Dr. Eyre, and published many papers on the subject.

He had been nominated for the Croonian Lectureship at the Royal College of Physicians for the past year, and chose for his subject "Acute Pneumonia." His colleague, Dr. Hale White, delivered the lectures last November from the rough notes which Dr. Washbourn had left. They give a masterly survey of our knowledge of the subject, dealing fully with the variations in the virulence of the coccus, in the modes of its growth, and with the preparation of an antipneumonic serum.

These lectures are mainly based upon their original observations. The lectures conclude with a series of experiments he had carried out with Dr. Pembrey on the channels which were taken in the lung by inhaled dust.

In 1897 he did an excellent piece of work in his "Bacteriological Report on the Maidstone Typhoid Epidemic," about which he had been consulted, indicating at once the probable source of the infection.

In February, 1900, he was chosen Physician to the Imperial Yeomanry Hospital which was established in South Africa at Deelfontein, where he organised with great success the medical side of the hospital. He afterwards proceeded to Pretoria, where he was gazetted Consulting Physician to Her Majesty's Forces in South Africa. For his valuable services he was awarded a C.M.G.

In June, 1901, he returned to England with his health somewhat impaired by the attacks of dysentery and of thrombosis from which he had suffered. He had several attacks of what he considered to be influenza, but in March he developed pleurisy with effusion, and died on June 20th from general tuberculosis at the early age of 39.

The accuracy and completeness of all his work was remarkable. He was an enthusiastic researcher, was exceptionally thorough in all that he did, deliberate when expressing an opinion, accurate in his mode of thought, and remarkably persistent.

The enthusiasm with which he threw himself into any sport that interested him, and the persistency with which he devoted his spare time to them, was equally striking. Boxing, bicycling, lawn-tennis, and skating in turns found him an ardent devotee.

He had a large circle of friends, and was most popular with all classes he came across, especially during the war. Many students were indebted to him for kindnesses often shown in a very practical manner.

For this tribute to the memory of a friend and colleague I am indebted to a member of the Staff of Guy's Hospital.

*Dr. John Curnow* died on July 5th, 1902, aged 56 years. He was Physician to King's College Hospital, and for more than twenty years Professor of Anatomy in the Medical Department of King's College. By his death the profession in London loses one of its best known men, a teacher of great repute, a physician of marked ability, and a man of much individuality and force of character. He succumbed to a very sudden attack of pneumonia, for he went round his wards at King's on Friday, July 4th, and died from syncope on the following morning.

Dr. Curnow was elected a Fellow of this Society in 1873. He acted as one of our Referees from 1884 till 1897, but held no other office, neither did he contribute to our 'Transactions.'

Dr. Curnow was a member of an old Cornish family, and was born at Towednack, Cornwall, in 1846. Throughout his life Curnow was devoted to his native county. His school education was obtained firstly at Penzance and subsequently at Bath. He commenced the study of medicine early as a pupil of Dr. Doidge, a well-known practitioner at that date in the west of Cornwall.

Gaining an Entrance Scholarship in 1862 at King's College, Curnow matriculated at the University of London in 1865, his name appearing in the list of honours. At King's he soon distinguished himself as an anatomist, obtaining the Exhibition and Gold Medal in Anatomy at the Intermediate M.B. Examination in 1868, winning also, at the same examination, the Exhibition and Gold Medal in Organic Chemistry, Materia Medica, and Pharmacy. He became M.R.C.S. in this year, and in 1869 he was appointed House Physician to King's College Hospital. At the final M.B. Examination in 1870 Curnow's name was again very prominently to the fore, for he won the University Scholarship and Gold Medal in Medicine, the University Scholarship and Gold Medal in Obstetric Medicine, and Honours in Forensic Medicine. He took the M.D. in 1871, gaining once more the Gold Medal. In 1873 he became M.R.C.P., and was elected to the Fellowship in 1878.

Curnow's proficiency in anatomy led to his being appointed Demonstrator of Anatomy at King's College, in succession to the late Mr. John Wood, and in 1873, on the death of the late Professor Partridge, he was elected his successor in the Chair of Anatomy at King's College. Few teachers could rival Curnow in knowledge and grasp of his subject, or in getting students to work at, and take a real interest in, the more scientific aspects of anatomy. His services as an examiner were in much request. Dr. Curnow was elected Assistant Physician to King's College Hospital in 1874, and Physician in 1890, a post he held at the time of his death, whilst the Professorship of Anatomy he resigned in 1896. For nearly twenty years he was Physician to the Dreadnought Hospital at Greenwich.

For many years Dr. Curnow was Dean of the Faculty of Medicine at King's College, and he took an active part in the Gresham scheme for the reorganisation of the University. For a quarter of a century Curnow was on the staff of the 'Lancet,' but naturally from this cause

his name is not very well known as an author, although he published his 'Gulstonian Lectures on the Lymphatic System and its Diseases,' and he also wrote some articles in Quain's 'Dictionary of Medicine.'

Although of a somewhat rough exterior, yet no more warm-hearted, genuine friend existed. He was greatly beloved by his colleagues and pupils, by all of whom he will be greatly missed.

*Professor Karl Gerhardt*, Privy Medical Councillor, Professor of Medicine, and Chief of the Second Medical Clinic at Berlin, a very distinguished German physician, noted especially for his skill and knowledge in diseases of the larynx, whose name came prominently before the profession at the time of the illness of the late Emperor Frederick, died on July 21st, 1901, at the age of 70, at his estate of Gamburg on the Tauber, in Bavaria, from a serious heart affection, which had already compelled him several months previously to give up his teaching and practical work at Berlin. Professor Gerhardt was elected a Foreign Honorary Fellow of this Society in 1896.

He was born at Speyer in 1833, studied at Würzburg, passed his M.D. examination in 1856, and soon afterwards acted as Assistant to Professors Bamberger and Rinecker, and later on as Assistant to the well-known Psychiatrist Griesinger, at Tübingen. In 1860 he established himself as "Privatdocent" at the University at Würzburg, the subject of his habilitation thesis being a paper on "The Position of the Diaphragm," which at once attracted general attention. It was probably owing to this very original monograph that already, in the following year, he was called as full Professor and Director of the Clinic for Internal Diseases to Jena. He accepted the call and remained at Jena until 1872, when he was recalled to Würzburg, where he remained until 1885. He was then called as successor to the late Professor Frerichs, at Berlin, where he worked, as already stated, until a few months before his death.

Shortly after he had entered upon his professional duties at Berlin he was consulted by the then German Crown Prince, being rightly considered one of the greatest living authorities on diseases of the larynx. It is a matter of history that he correctly diagnosed the case and proposed the proper treatment, but that his views unfortunately were superseded. Gerhardt unflinchingly, and without a word of complaint, bore the ignominy which was heaped upon him, until the ultimate development in the illustrious patient's case showed that he had been right from the beginning.

Whilst being a great general physician, he cultivated particularly affections of the chest, throat, and children's diseases, and in each of these branches was a recognised authority throughout the world. He was a fertile author, and all his writings were distinguished by extreme brevity, clearness, and accuracy of expression. As a teacher he inspired his assistants and students with genuine love for their work, as well as with admiration for their teacher. His verbal expression was distinguished by the same qualities which were characteristic of his literary style.

As a man, he was a gentleman in the finest sense of the word: not soft-spoken; indeed, often rather rough, sceptical, and ironical; but actuated in everything he said or did by the highest sense of duty and honour, and by genuine love for his science.

*Mr. James Thomas Ware* died at Tilford, near Farnham, on July 30th, 1903, aged 85 years. He cannot truly be said to have been ever much engaged in the practice of his profession. Not very good health as a young man has been given as one reason for his early retirement, but probably the possession of landed property and ample private means were more potent factors in his decision.

Mr. Ware was for very many years prior to his death a Non-resident Fellow. He joined the Society in 1846, but had not been in any way associated in its work.

James Thomas Ware was the eldest son of the late Mr.

Martin Ware, of Tilford, and the grandson of Mr. James Ware, F.R.S.; both of these gentlemen practised as ophthalmic surgeons, being eminent in their day. Mr. J. T. Ware entered as a student of St. Bartholomew's in 1835, and was a fellow-student of the late Sir James Paget, of the two Monros, Theodore and Henry, as well as of Luther Holden. After qualifying, he was appointed one of the House Surgeons, and subsequently he became a Governor of the Hospital. In one of the early years of his professional life he went on to the Continent, and studied at Paris, Vienna, and Berlin. In 1845 he became F.R.C.S. by examination.

Mr. Ware was one of the Founders of the present well-known Metropolitan Convalescent Institution, of which he was a warm supporter and friend until advancing years and infirmity compelled him to give up coming to London. Mr. Ware held an influential position in the Society for the Relief of Widows and Orphans of Medical Men.

The larger part of his life was passed at Tilford in following the usual avocations of a country life, but without the slightest taint of ostentation. He was Chairman of the Board of Guardians of the Farnham Union, and in many similar ways he did most useful work in his locality. It was innate with him to wish to relieve distress and to benefit the poor, whilst he was greatly esteemed by all his neighbours. Mr. Ware had not ever married.

*Mr. William Henry Hayward* died in Manchester, to which city he had only very recently removed from Leeds, where for some five years he had practised. He was in his sixty-ninth year, and died of heart disease on August 6th, 1902.

Mr. Hayward was elected a Non-resident Fellow in 1861. He had not contributed to the Society's 'Transactions.'

William Henry Hayward received his medical education at Queen's College, Birmingham. He was a diligent student, and eventually came out as medallist in clinical

medicine and clinical surgery. He qualified in 1856 as M.R.C.S.Eng., and in 1863 took the L.S.A.Lond. He was elected House Surgeon at the Queen's Hospital, whilst later he settled at Oldbury, practising for many years in that town, and being its Medical Officer of Health.

Mr. Hayward took a great interest in geology, and wrote many papers on the subject; one of them, published in 1864, related to the discovery of remains of the *Elephas primigenius* at Oldbury. A man of artistic, literary, and musical tastes, he was a most genial companion, and his death is much regretted by all who had the pleasure of knowing him. At the time of his death Mr. Hayward was in his sixty-ninth year; he was a widower, and has left a large family.

By the death of *Professor Virchow* at Berlin on September 5th, 1902, in his 81st year, the Society loses the most famous as well as the oldest, in point of election, of its Foreign Honorary Fellows, since he was selected for this honour so long ago as 1856, shortly after the publication of his celebrated work on 'Cellular Pathology.'

Rudolph Ludwig Karl Virchow was born on October 13th, 1821, at Schiesselbein, near Stettin, and he was the son of one Karl Virchow, a small shopkeeper. His early education was obtained at a school in this town, but at the age of thirteen he was sent to the gymnasium at Cöslin. At this period of his life Virchow appears to have shown a quite remarkable aptitude for languages, ancient and modern alike. After passing his "Abiturienten" Examination he joined the Friedrich-Wilhelm Institut for the professional education of Prussian Army Surgeons, and took his degree at Berlin University in 1843. Even at this early age his intellectual powers and his force of character had won recognition from his superiors, for he was amongst those who by way of distinction were commanded to do scientific work at the Charité Hospital. Shortly after he was made Assistant to the Prosector of Anatomy, Robert Froriep, whom in 1846 he succeeded.

The following year Virchow, having qualified as "Privat-docent," received the appointment of External Lecturer in Pathology. This post gave Virchow the opening for research in his special branch of study, and may be taken as the starting-point of his great career. Thus it came to pass that at quite an early age he became famous and his name everywhere mentioned as one of the celebrities of the civilised world.

Shortly after his appointment he founded the renowned 'Archiv für pathologische Anatomie und Physiologie und für klinische Medicin,' and he continued to edit it for upwards of fifty years.

In 1848 Virchow was deputed to investigate the circumstances of a severe outbreak of typhus fever in Silesia. In his report, beyond stating the medical features of the epidemic, he denounced in vigorous terms the system which tolerated the insanitary and degrading conditions in which the poor lived. This report created a great sensation, whilst to Virchow the knowledge thus gained of the miseries endured by the lower orders of Society gave him a new interest. It caused him to take up sanitation in general, and municipal sanitation in particular. He threw himself with characteristic ardour and fearlessness into the political arena. Then followed the troublous epoch of 1848, and for a time Virchow was compelled to leave Berlin. He received an opportune call, however, to Würzburg, and there, whilst Professor of Pathology, he commenced to publish his *magnum opus*, 'Die Cellular Pathologie,' which, however, was not issued as a completed work until 1858, and after he had been recalled to Berlin as Professor of Pathology, the Government acceding to Virchow's request to equip a complete pathological institute and to place it under his sole control. In this post he worked for the remaining years of his long life with untiring energy, and yet with simple, straightforward devotion to the work he loved so dearly. During 1899 he had the satisfaction of seeing his magnificent pathological collection suitably



housed in the splendid museum at the new Charité Hospital.

Only a brief reference need be given on this occasion to Virchow's political career. Public life had attractions for him. He became a member of the Municipal Council of Berlin, and had a seat in the Prussian Chamber, to which he was elected in 1862. Now he realised that the opportune moment had arrived for pressing forward sanitary measures and plans for alleviating the deplorable state of the working classes. Virchow was the guiding spirit in carrying out far-reaching schemes of sanitation, such as water supply, drainage, and hospitals for various forms of disease. In all of these Virchow showed remarkable ability as an organiser, and also that at all events he was no simple philosophic dreamer. It was owing to Virchow's initiative and sagacity, quite as much as to his knowledge of hygiene, that Berlin was rescued from its evil reputation of being a disease-ridden city and converted into one of the healthiest of the capitals of Europe, whilst some of its principal institutions are standing monuments of his energetic care for the sick, afflicted, and poor.

In the Prussian Diet Virchow rose to be the leader of the Radical Party, and was for many years Chairman of its Finance Committee. It was whilst occupying these positions that the memorable event happened of his receiving a challenge from the mighty Bismarck to fight a duel. This proposal, with characteristic *sang-froid*, the professor rejected.

In the campaigns of 1866 and of 1870-71, Virchow entered heart and soul into the preparation and organisation of the army ambulance system.

It has to be borne in mind that at this period, as well as all through his long tenure of the professorship, the duties of this office were not only his chief preoccupation, but were the pride and joy of his life. As regards his conception of his professorial work and object, I may fitly give a quotation in full from an obituary notice

in the 'British Medical Journal' of September 13th, 1902:

"Virchow's great task was to free medical knowledge from the conflicting dogmatism and arbitrary hypotheses which encumbered it, and to establish its leading principles irrefutably by a process of sound induction from actual observations and experiments. At the commencement of his career the humoral theory was dominant, and the explanation of morbid processes was sought either in the nerves, the blood, or the exudations of the body. So long as these views prevailed it was impossible to form a true appreciation of the brilliant discoveries of pathological anatomy which had been made in the Vienna school, and hence Rokitansky, their leading exponent, whose theory of crases and dyscrasias of the blood was supposed to explain anatomical lesions, was one of the first objects of Virchow's attack. Virchow's position is well defined in his introduction to the first volume of his 'Archiv,' published in 1847, and written at a time when his own labours had already accomplished enough to give him a grasp of the problem before him: 'The rôle of pathological anatomy as a dogmatic science is at an end; for each individual law we must have the proof, clearly recognised, and carrying personal conviction. But where are the proofs to come from when the entire argument begins with a hypothesis?' The whole system, he goes on to say, must be changed, and the work of observation and experiment must take its place. 'Pathological physiology will then gradually develop itself, not as the mental product of individual enthusiasm, but as the result attained by many investigators from the outcome of laborious research. Pathological physiology will then be recognised as the stronghold of scientific medicine to which pathological anatomy and clinical observation form but the outworks.' In these sentences is to be found the dominant idea which inspired Virchow's work and led to the results which we must now consider.

“Virchow's first important labours were upon the nature of blood diseases. Commencing, immediately after he took his degree, with an investigation into the nature of phlebitis, he followed up these researches with a series of brilliant discoveries which alone would entitle him to a position in the front rank amongst the pathologists of the last century. The conditions of vascular inflammation, the causes of thrombosis and embolism and their relation to infection, were investigated; pyæmia was defined and clearly distinguished from leukæmia, with which it had previously been confused; and a valuable insight was given into the nature of the latter disease.

“Soon after the commencement of his ‘Archiv’ he began to publish articles in that journal which foreshadowed the appearance in 1858 of his ‘Cellular Pathology.’ In that work, which is the foundation of modern pathology, the researches of Schleiden and Schwann upon the cellular structure of vegetable and animal organisms were confirmed and further elaborated, and the part which the cell plays in pathological processes was established for the first time. Recognising the value of Schwann's theory as showing that all physiological activity must be referred ultimately to the cell, that the cell is the seat of life, and that vital manifestations are due to its activity, Virchow showed that the same principle was equally valid for pathological relationships, and that in an abnormal modification of these same cellular activities is to be found the explanation of disease. But Virchow did not simply adapt Schwann's theories to his own subject; he reconstituted them. ‘According to Schwann,’ he declared in his lectures, ‘the intercellular substance was the cytoblastema, destined for the development of new cells. This I do not consider to be correct.’ He substantiated his object by proving that the theory of cell-formation out of a conglomeration of granules in a blastema was erroneous, and must be replaced by his now famous dictum, *Omnis cellula e cellula*. The theory that every cell arises from a pre-existing cell, together with the recognition of the

cellular character of the connective tissues, revolutionised pathology by introducing the new principle that all pathological cell-formations arise from the division of normal cells. The scientific bearings of these discoveries are best described in Virchow's own words. In his Croonian Lecture delivered before the Royal Society in 1893, he traced the sequence of ideas which had led up to his cellular theory, and expressed its results in the following terms:— 'The begetting of a new cell from a previous cell supplemented the reproduction of one individual from another, of the child from the mother. The law of the continuity of animal development is therefore identical with the law of heredity, and this I now was able to apply to the whole field of pathological new formation. I blocked for ever the last loophole of the opponents, the doctrine of specific pathological cells, by showing that even diseased life produced no cells for which types and ancestors were not forthcoming in normal life.' "

Sir Felix Semon, in his charming "Personal Reminiscences" in the same issue of the 'British Medical Journal,' thus describes the work the Professor would deal with in one day:

"He would conduct an examination from 8 to 10 a.m., would superintend a microscopic class from 10 a.m. to 12, would lecture from 12 to 1 p.m., would be in the Reichstag from 2 to 5 p.m., in the Town Council from 5 to 6 p.m., in some committee meeting of the Prussian Parliament from 6 to 7 p.m., and preside at the meeting of the Berlin Medical Society, or at the Anthropological Society, or deliver some popular address, or again do committee work from 7 to 9 p.m. Well may I be asked: But where did his meals come in? Where did all his enormous original and editorial literary work, his correspondence, his family life, come in? Well, that is the wonder of all who had the privilege of coming near him. One of the explanations of his superhuman activity is that he required infinitely less sleep than most mortals. When I was a student at Berlin there was a sort of legend that he never slept more

than five hours. When later on I had the great good fortune of being admitted into his family circle, I asked whether there was any truth in that legend, and to my surprise learned that often it fell far behind the truth, and that more than once he had, when under—what was for him—exceptional pressure of work, not gone to bed at all, but worked through the whole night! Honour to a man who thus sacrifices himself for the public weal, and every allowance for his unavoidable unpunctuality! Strait-laced people may object that a man ought not to undertake more work than he could punctually fulfil; but whilst this in the case of ordinary mortals is true enough, the reply in Virchow's case is that the world in many respects would have been much poorer had this wonderful man limited himself to the ordinary professor's work and not shed the lustre of his personality, of his lofty mind, of his inexorable logic upon politics, municipal work, anthropology, ethnology, and a hundred other branches of human thought. If a few details of his routine work necessarily suffered from his physical inability to be in several places at once, the whole human race benefited from the application of this master mind to so many different human interests."

Again from Sir Felix's obliging pen I can present a sketch of Virchow as teacher:

"The great characteristic of Virchow's teaching was his insistence on doing everything methodically. There was no looking after interesting or important things first in a post-mortem examination, and the rest being done in a slipshod fashion; every step had to be taken in an invariable, well-thought-out order, and everything was to be considered equally important. Whilst some might call this pedantic, there can be no doubt as to the value of these principles when post-mortem examinations are being made by practitioners to whose share it only occasionally falls to do this, and particularly in forensic cases.

"As a lecturer he was equally methodical. When lecturing on selected chapters of pathology no detail

appeared to him too insignificant not to be considered at full length, and he particularly insisted, when demonstrating specimens, on distinguishing variations of colour, which were indistinguishable to a large number of his audience.

"Although his delivery was somewhat monotonous and dry, there was a charm about it, resulting probably from the conviction, which impressed itself more and more as he proceeded upon his hearers, that they listened to an accomplished master of his subject, and from the admirable clearness with which the most difficult subjects were explained by him. On rare occasions, however, when he felt himself to be the spokesman of the medical profession in matters of supreme importance, his voice gained an almost trumpet-like sound, and his delivery on such occasions was most forcible. Thus those who were present at the delivery of his address on vivisection before the International Medical Congress of 1881 will remember how he rose to the occasion, and how every sentence was delivered with the utmost decision, and that his voice, which penetrated into every corner of St. James's Hall, roused the audience to enthusiastic applause.

"When lecturing to large audiences of either professional men or of a mixed character, the encyclopædic knowledge of the man became most conspicuous, although always clad in such modest and simple language as if all he said was self-understood.

"On these occasions, however, he often lost his sense of time and overrated the receptive capabilities of his audience. When he wished to bring forward a subject which at the time engrossed his whole attention, the dimensions of his lecture sometimes exceeded by far the usual length of time accorded to such expositions, and however marked the signs of fatigue and impatience were after he had been listened to respectfully for a long time, he would mercilessly read on till he had finished all he had to say. On the very last occasion when he gave such an exposition before a large audience, *i. e.* on the occasion of

his eightieth birthday, a witty colleague of his was overheard to observe, when the audience were half dead after a lecture and demonstration which had occupied more than two hours in the middle of the day, when ordinary mortals take their lunch : 'I am sure Virchow has only attained such a grand old age because he has never had to listen to such lectures.'

"It need, however, not be said that his little weaknesses as a lecturer detracted as little from the universal filial piety and veneration with which he was regarded by his pupils as his even more strongly marked peculiarities as an examiner."

Professor Virchow paid many visits to England. He never concealed his admiration of the freedom in the widest comprehension of the term which this country enjoys, and which it extends to the law-abiding of all creeds and nationalities.

Amongst his most memorable visits to this country mention should be made of the International Medical Congress held in London in 1881, of his delivery of the Croonian Lecture of the Royal Society in 1893, on "The Position of Pathology among the Biological Sciences," in which with all his wonted lucidity he described the advances pathology had made since the time of Harvey. The lecture followed the award of the Copley medal for his researches in pathology, pathological anatomy, and prehistoric archæology. In acknowledging its receipt Virchow said that "its significance far exceeds the distinctions which the changing favour of political powers is accustomed to bestow." In 1898 Virchow delivered the Huxley Lecture at Charing Cross Hospital on "Recent Advances in Science, and their bearing on Medicine and Surgery." A day or two later a dinner was given in his honour by the profession in this country, Lord Lister presiding.

In 1897 the jubilee of his first teaching appointment and of the foundation of the 'Archiv' were commemorated at Berlin. On this occasion, as also in 1901, when his

eightieth birthday was celebrated, it seemed as if to the little, grey, apparently impassive, yet keenly vigorous man, advancing years had no effect in dimming either his bodily activity or his intellectual ardour. At the jubilee gathering Lord Lister, on behalf of the Royal Society and this, among other learned bodies of the United Kingdom, said, "All these bodies join in the recognition of your gigantic intellectual powers, in gratitude for the great benefits which you have conferred on humanity, and in admiration of your personal courage, your absolute uprightness—the courage which has enabled you always to advocate what you believe to be the cause of truth, liberty, and justice; and of that genial nature which has won for you the love of all who know you."

The closing scene of this grand career was nevertheless at hand, for on January 5th, 1902, in alighting from a tramcar in motion, he fell heavily and sustained an intra-capsular fracture of the neck of the femur. He convalesced to the extent that he was able to move about on crutches; yet it was evident to all about him that his constitution had received a shock from which he would never recover. A gradually increasing weakness supervened, and although he was removed to Harzburg, the mountain air failed to invigorate him; so he was brought back to his house in Berlin, where on the 5th September he passed away.

I cannot forbear, in concluding this notice of the late Professor Virchow, from quoting a paragraph from the 'Times' obituary notice (September 6th, 1902):

"The name of Virchow has become familiar to the man in the street, but probably few even of those who are best able to appreciate his work realise its full extent, so multifarious was his activity, so versatile his genius. The rule which warns us that versatility is a snare, and that a man can only hope to excel in one thing, is sound enough for mankind in general, but now and then the ages produce an exception. Virchow was such an exception, and one the more remarkable because the ever-



increasing specialisation of our time makes it more and more difficult for a single brain to do first-class work in more than one field of activity. Those who attempt more are apt to be mediocre in all, or else they have something morbid—some touch of insanity in the proper sense of the word—in their constitution and die young, prematurely burnt up by the fire of their own energy. But this singular man attempted many things and was mediocre in none, and so far from having any morbid strain about him, he devoted a very long life to arduous and incessant labour, in which complete sanity of judgment was, perhaps, the most conspicuous feature. Darwin, Pasteur, Helmholtz, were pure men of science who eschewed the turmoil of public life; he stands by their side as a great pioneer in the most obscure of all sciences; but he also led a political party for years and crossed swords on equal terms with one of the greatest statesmen of the century, and at the same time he accomplished more practical work in social and administrative reform than any other individual of his time. Yet he remained free from the taint of ambition and self-seeking. Perfectly simple and modest, he coveted no honours, nor could any decorations have added to the lustre of his name. He respected himself and others, but most he respected truth and justice. A great controversialist and fearless in utterance, he never hesitated to speak boldly and strongly without any regard to the eminence of his opponent or the prejudices he assailed; and this outspoken manner made enemies, as it generally does. But his mind was always open, his judgment clear and undisturbed by prejudice. If he held strong opinions and expressed them strongly, it was because they were founded on knowledge and reason. Thus he did not hesitate to run counter to the current of popular and professional opinion and of Court favour when his distinguished colleague, Robert Koch, made the world gape by announcing the famous cure of consumption. Virchow calmly examined the evidence and pronounced against it on definite grounds. On the

other hand, when a few years later the medical profession—having burnt its fingers once—was timidly boggling at the sister discovery of antitoxin for diphtheria, he flung the weight of his authority into the opposite scale with equal firmness, and boldly declared that it was the bounden duty of every practitioner to use the new drug. The whole world shares with Germany the loss of this calm, wise mind, with its brilliant endowments, its immense erudition, its lofty purpose, and inspiring example.”

*Dr. Daniel Burton Kendell*, J.P., M.B.Cantab., died at his residence, Thornhill House, Wotton, near Wakefield, on October 1st, 1902, on his 84th birthday. Dr. Kendell had spent more than fifty years at or in the neighbourhood of Wakefield, occupying a leading position not only as a medical man, but equally as a large-minded, active citizen.

Dr. Kendell became a Non-resident Fellow in 1848, but had never taken any part in the affairs of the Society.

Daniel Burton Kendell was born in 1818, and was educated at the Leeds Grammar School. He proceeded to Caius College, Cambridge, in 1838. Kendell was a keen athlete, and so good an oarsman that he secured a place in his College boat and shared in the triumph of landing it head of the river.

After taking his B.A. he entered at St. George's Hospital, and became M.B.Cantab. in 1847. He married and settled at Wakefield in 1848; later on he was elected Physician to the Wakefield Dispensary, which subsequently became merged in the Clayton Hospital. On his retirement from this office in 1859 he was elected a Vice-President of the Hospital.

Dr. Kendell was made a J.P. for the West Riding of Yorkshire in 1862, and took a very active share in county business. On the creation of County Councils he was awarded aldermanic honours in the West Riding Council,

and selected to be Chairman of its Sanitary Committee. He was also an active member of the General Asylums, the Wakefield Sub-Asylum, and the Law and Parliamentary Committees. In addition, he was a member of the River Board and of the Standing Joint Committee.

Up to the spring of 1902 Dr. Kendell was able to devote much of his time to a fairly active discharge of these public duties; lately, however, his great age had told on his vitality. Dr. Kendell will be greatly missed, and in Wakefield his memory will be long cherished as one of the best types of England's country gentlemen.

*William Bird*, a well-known and greatly respected resident of Hammersmith, who for very many years had identified himself with the advancement and success of the West London Hospital, died on October 4th, 1902, at his residence, Bute House, Brook Green, in his 71st year.

Mr. Bird was elected a Fellow in 1856; he had not, however, held office, neither had he contributed to the Society's 'Transactions.'

Mr. William Bird was born in 1832, the only child of William Bird, J.P., D.L., of Bute House, Brook Green, a gentleman of considerable fortune. At first intended for the Army, he was educated by a private tutor, but ultimately entered at St. George's Hospital. After qualifying he started practice in George Street, Hanover Square; but he never needed to earn his living, and on the death of his father in 1864 he retired, and henceforth lived at Bute House, Brook Green, a handsome house with extensive grounds in which he kept deer and other animals.

The occupation of his life now became mainly legal. He was an enthusiastic Middlesex magistrate, earnestly devoted to his duties on and in connection with the Kensington Bench, where he presided for many years.

He still retained a close association with his own profession through the Chairmanship of the West London Hospital, which he held for more than thirty years. That institution had been founded in 1856 as a dispensary,

through the exertions of his father, assisted by the late Mr. Ralph Ainsworth, M.R.C.S., Sir John Phillipart, and by the then Duke of Devonshire. Bird was himself on the surgical staff from the commencement, and died "Consulting Surgeon." In the earlier years of his chairmanship he gave to and collected considerable sums of money for the West London, and finally left it £1200 and the residuary legateeship of the bulk of his property in the rather remote contingency of his nephews' dying without issue. He was a widower, without children.

William Bird was a tall man with rather handsome features, always carefully and well dressed, and watchful that his carriage, horses, house, grounds, and other property should be good in appearance and of solid value. He used his great influence in the elections at the hospital with a real desire for the interests of the place, his first principle being to make it what he called "a gentlemanly hospital." He was the reverse of progressive, and generally opposed every development of the hospital, on the score of expense, until the march of events made opposition hopeless. He was kind-hearted and fond of exercising his very considerable patronage, especially for the benefit of the young and struggling.

He died of cerebral tumour. The exact position and relations of this tumour were only realised at an autopsy, for which he had left written instructions.

*Dr. David Little*, an eminent ophthalmic surgeon with a wide-spreading reputation, and that not only around Manchester, where he had practised for nearly forty years, died from pernicious anæmia on November 27th, 1902, aged 62, at Congleton.

Dr. Little was elected a Non-resident Fellow in 1872.

He was born in Lockerbie, Dumfriesshire, in 1840. When sixteen years old he matriculated at Edinburgh University, and graduated as M.D. in 1859 at the age of nineteen. After spending a few years as an Assistant, he obtained, in 1863, the appointment of House Surgeon

and Secretary to the Eye Institution, which subsequently became the Royal Eye Hospital, and in 1867 Dr. Little was elected on to its Surgical Staff. In 1878 he became Lecturer in Ophthalmology at Owen's College, and in 1882 was appointed Ophthalmic Surgeon to the Manchester Royal Infirmary.

In 1901 he was elected President of the Ophthalmological Society of the United Kingdom. Dr. Little was the first provincial surgeon to receive this distinction, and he was very justly proud of it.

At the beginning of the year 1902 it was only too manifest that his splendid constitution had begun to decay. He aged rapidly in appearance and manner, and by many was thought to be years in advance of his real age. A rest from public and private work and a sojourn in Egypt did not, unfortunately, improve his condition; he steadily got weaker, until it was found imperative for him to give up the idea of being present at the meeting of the British Medical Association in Manchester this year, and of presiding in the Ophthalmology Section. An autumn trip to Norway was then undertaken under the most unfavourable climatic conditions, and he seemed to have suffered much from the cold and discomfort of the sea voyage. For the last few months his appearances in Manchester were rare, and his rapidly increasing weakness finally forced him, after a manful struggle and the exhibition of great fortitude, to take to his bed in October last.

His writings were few, probably owing to the exigencies of an enormous practice, but what he did write was absolutely reliable, clearly expressed, and to the point; this is well seen in his last contribution to the study of glaucoma, embodied in his Presidential Address to the Ophthalmological Society of Great Britain. A careful and expert operator, a man of shrewd powers of diagnosis, he was an implacable foe of charlatanism and self-advertisement, while at the same time his kindly nature was always perhaps too ready to find excuses for the ethical lapses of others,

even when his own interests were being assailed. Having acquired in early life the habits of frugality and temperance in all things, his private life was marked by great simple-mindedness and avoidance of ostentation and show. His grave and often solemn demeanour masked very slightly the warmest of hearts and the kindest of natures. Absolutely straightforward and strictly honourable, he was a most pleasant colleague, and one readily accessible at all times to those who required his cautious and well-weighted words of advice and assistance.

Dr. Little married a daughter of the late Anthony Shaw, Esq., of Buglawton, Cheshire, who, with one son and two daughters, survives him.

*Mr. Edward Unwin Berry*, who died on December 5th, 1902, in his 92nd year, had carried on a laborious general practice for upwards of fifty years, first in James Street, Covent Garden, later in Gower Street, and finally at Sherriff Road, West Hampstead, where he died.

Mr. Berry was elected a Fellow in 1845, and his firm support of and goodwill towards the Society was shown in many ways, and notably in that he bequeathed it a legacy of £300; and although Mr. Berry never actually held office, he received nomination to the Council in 1897, which failing eyesight, however, prevented his accepting.

After Sir John Simon Mr. Berry was the next senior Fellow of the Society, whilst, in point of age, he was probably its oldest Fellow.

Mr. Berry was born in 1811, and received his medical education at the London Hospital Medical School. He married in 1838. Whilst working almost night and day for the first twenty-five years of his professional life, he yet found relaxation in music, painting, and the study of languages. He possessed in his younger days a good tenor voice and was an accomplished flautist, and he played up to the age of ninety, whilst when seventy he commenced the study of Greek and succeeded in mastering it.

Mr. Berry was a man of dogged perseverance and industry, whilst to many he was a kind friend and sound adviser. In his old age failure of sight was a grievous affection, because of the enforced idleness which it entailed. Some two months before death increasing weakness alone made him remain in bed, and at the end he passed away quite peacefully.

*Francis Manley B. Sims*, well known and very prominent for the last quarter of a century as a gentleman carrying on probably the largest general practice in the West End of London, died very unexpectedly on December 10th, 1902, aged 61 years.

Mr. Manley Sims was elected a Fellow in 1892. He neither held office nor made any contribution to the Society's 'Transactions.'

Manley Sims was born in 1841 at Stoke-by-Nayland, Suffolk. His father was the Rev. Frederick Sims, Rector of West Bergholt, Essex, and at one time Fellow of Exeter College, Oxford. He was educated at the Grammar School of Colchester, and when sixteen was apprenticed to Mr. Young, practising in Sackville Street.

One who knew Manley Sims well from his student days onwards has kindly supplied me with the following particulars of his career :

"Throughout his professional career," he says, "the most noticeable characteristic about Manley Sims was his indefatigable energy and perseverance, and his great power of work. During the time he was a student at St. George's Hospital he was also assistant to a medical man who practised in Sackville Street, and the portion of the day that was not occupied in attending lectures, dissecting and studying in the wards, was devoted to the work of his assistantship, so that he was obliged to rise at five o'clock in the morning to do his necessary reading and prepare for his examinations. This, no doubt, led to the habit, which stuck to him throughout life, of early rising.

"During the whole of the time he was engaged in private practice he might be seen in his brougham at half-past seven or eight o'clock in the morning, paying an early round of visits to his more serious cases before breakfast.

"After he had served his year of office as House Surgeon at St. George's Hospital, he was appointed Demonstrator of Physiology in the Medical School, and not content with teaching what he himself knew, he worked hard to increase his knowledge and render himself more capable of instructing his pupils. It so happened that the writer of these lines had a large collection of microscopical sections of the normal human body, and Sims would often turn up at nine or ten o'clock at night, just freed from a hard day's work, with a request that he might be allowed to examine the specimens and work at them.

"The same habits of diligence and perseverance followed him throughout his active life. He was always busy about something, and always anxious to acquire some fresh knowledge. On one occasion the writer was driving with Sims in his brougham, which always contained a stock of books, and he incidentally took up one of these and found to his surprise that it was 'Euclid.' He made some remark of astonishment at finding such a book in such a place, and was met with the reply, 'Oh, I take everything in its turn. I have been lately working at my classics, and now I am going to have a turn at mathematics. I shall work through all those propositions before I have done with it.'

"During the earlier part of his professional career, before he joined the firm of Fuller and Hammerton, he carried on the practice of his old master in Sackville Street, who was now dead; and in addition to this and the work connected with his teaching of physiology at St. George's Hospital, he found time to study diseases of the skin at the hospital at Blackfriars, to which, for some time, he was Assistant Surgeon; and diseases of children at the hospital in Great Ormond Street, where he was Clinical Assistant. No doubt the special knowledge he obtained at these two hospitals



helped him much, and proved of great service to him in his future practice."

Mr. Manley Sims leaves a widow and three children. Mrs. Sims is a daughter of the late Dr. Fuller, Physician to St. George's Hospital.

*Dr. Samuel Fenwick*, who will be chiefly remembered as a physician skilled in the treatment of disorders of the digestive system, died on December 11th, 1902, in Harley Street, where he had practised for well nigh forty years, in his 82nd year.

Dr. Fenwick was elected to the Fellowship of this Society in 1863. He was a Referee from 1882-96, and he made four communications to the Society's 'Transactions':—Upon the condition of the gastric and intestinal mucous membranes in scarlatina, On the existence of lung tissue in the expectoration of persons affected with phthisis, The morbid appearances of the stomach and intestines after death from cancer, and On the amount of the sulphocyanide of potassium in the saliva.

Samuel Fenwick was born at Earsdon House, Northumberland, in 1821. At the early age of fourteen he was apprenticed to the Royal Infirmary, Newcastle-on-Tyne; at twenty-one he qualified, passing the M.R.C.S.Eng., and a few years later he obtained the M.D. of St. Andrews. Having to make his own way in life, Dr. Fenwick commenced general practice at North Shields, and whilst thus engaged he published 'The Nature and Prevention of Disease' and 'Certain Affections of the Throat of a Chronic Character.' These works brought him into repute, and in all probability led to his appointment as Lecturer on Pathological Anatomy at the Durham Medical School, whilst later he was appointed an Examiner in Medicine at the University of Durham, which body, in 1859, made him an honorary M.D.

For a few years Dr. Fenwick practised as a consulting physician in Newcastle, but in 1862, being then 41 years of age, he settled in London. He took the M.R.C.P., and

he was elected F.R.C.P. in 1870. He was appointed Assistant Physician to the Victoria Park Hospital for Diseases of the Chest, whilst a few years later he was elected on to the Staff of the London Hospital. Dr. Fenwick published in 1869 'The Student's Guide to Medical Diagnosis,' which has gone through nine editions; whilst his 'Outlines of Medical Treatment,' published in 1879, has run through four editions. His numerous contributions to medical literature have been chiefly on subjects connected with the digestive organs.

Of Dr. Fenwick's zealous work as a physician and clinical teacher at the London Hospital I am indebted for the following appreciation sent to one of the late Dr. Fenwick's colleagues by an old House Physician :

"Those of us who had the privilege of working for Dr. Samuel Fenwick, either as Clinical Clerk or House Physician, and have since gone into general practice, will look back on the time as one of the most valuable periods of our medical training.

"If I were asked to name the feeling with which he inspired us I should say it was reverence. He was our revered teacher, for these reasons: his great clinical wisdom and his unique power of imparting his knowledge to the least of us evoked our admiration; while his courteous, kindly manner to his patients and ourselves won our affection.

"The most inexperienced of Dr. Fenwick's clerks was at once made to feel that he was, in a sense, a colleague in the care of the patient, and that any facts which he could bring forward, founded on correct observation, were *valued* by his 'Chief.' This was the best incentive to work that he could give us, and his relations with his House Physician were on the same happy but even more intimate basis.

"From the time Dr. Fenwick entered his wards till he left them it was well to keep ears and eyes open. The man who came armed with note-book and pencil hoping to be supplied with neat lists of the causes of any disease.

infallible diagnostic signs, and abbreviated treatment, 'suitable for examination purposes,' might be disappointed.

"Dr. Samuel Fenwick's aim was not to teach us how to get through examinations, but by precept and example to show us how to approach the sick so as to gain their confidence and co-operation; how to proceed with our examinations; how to weigh the evidence in forming our opinion as to the seat and character of the disease; and finally, how to proceed to the patient's cure or alleviation.

"If we had paid close attention to the steps of his examination and had taken pains over our own part of the case, then he by his wonderful power of expression could take us with him through all the delicate stages of reasoning which a case for diagnosis presents. He not only made us the receiver of his thoughts, but the companions of his thinking. We were, most of us, going to be general practitioners, and to us Dr. Samuel Fenwick seemed to embody all that was best in a clinical physician, G.P., and consultant.

"The writer was one of the last to have the privilege of working for Doctor Fenwick at the 'London,' and in his memory, as in many another's, a picture will remain for long. It is Dr. Fenwick, standing at the bedside, his kindly, expressive face alight with enthusiasm, giving us without stint of the best that is in him, using language as simple as it is effective, without raising his voice above that which is suitable to a sick room, riveting the attention of us all.

"A great teacher and a great doctor."

*Edward Tegart* died on January 9th at the age of 81, at 60, Scarsdale Villas, Kensington, where, since retiring from active professional work, he had lived. Mr. Tegart was a Roman Catholic, and his practice lay naturally chiefly amongst his co-religionists, but he was universally esteemed by the profession and by a wide circle of friends.

Mr. Tegart was elected a Fellow of the Society in 1859.

He served office as a Member of Council in 1888-9. He did not contribute to the Society's 'Transactions.'

Edward Tegart received his medical education at St. George's Hospital, and when qualified joined his cousin—another Mr. Edward Tegart—in general practice in Jermyn Street. After the death of his cousin he carried on the practice alone. He was for many years Surgeon to St. John's and St. Elizabeth Hospital in Great Ormond Street, to which, at the time of his death, he was Consulting Surgeon. He was also for many years a Vice-President of the Society for the Relief of Widows and Orphans of Medical Men.

By the death of *Sir George Gabriel Stokes*, Bart., Master of Pembroke College, F.R.S., at Cambridge on February 1st, 1903, in his 84th year, England has lost its most eminent living mathematician; the University of Cambridge one of whose scientific and scholarly attainments it was justly proud; and this Society almost its senior Honorary Fellow, for this distinction was conferred on Sir George Stokes in 1873, Sir Joseph Hooker alone taking precedence of him.

George Gabriel Stokes was born at Skreen, county Sligo, on August 13th, 1819. His parents were the Rev. Gabriel Stokes, rector of Skreen, and Elizabeth, daughter of the Rev. John Haughton, rector of Kilrea. He was educated at Dr. Wall's school, Dublin, and at Bristol College. Subsequently he proceeded to Pembroke College, Cambridge, where he graduated as Senior Wrangler in 1841 and was elected to a Fellowship, which he vacated on his marriage in 1857, but to which he was re-elected under the new statute in 1869. He was appointed Lucasian Professor of Mathematics in the University in 1849, and was elected a Member of the Royal Society in 1851. In the following year he was awarded the Rumford Medal in recognition of investigations regarding the refrangibility of light. He was appointed one of the secretaries of the Society in 1854, and, after numerous contributions to the 'Transac-

tions' of that and other learned bodies, he became President of the Royal Society in 1885, a post which he held until 1890. In 1889 he was created a baronet in reward for his services to science, which were freely recognised abroad as well as at home, and brought him, among many other distinctions, the Prussian Order, *Pour le Mérite*. He received honorary degrees from his own University, from Oxford, Edinburgh, Dublin, Glasgow, and Aberdeen. Sir George presided at the Exeter Meeting of the British Association in 1869, and in the following year he was appointed to serve on the Cambridge University Commission.

"The celebration of the jubilee of Professor Stokes, the crowning honour of a distinguished career, took place three and a half years ago. Other Professors of the University had held their professorships more than fifty years, but this was the first occasion upon which the University had officially celebrated the event. With no disparagement of the claims of others to a similar celebration, it was felt that no professor had attained so wide-spread a reputation as Sir George Stokes, and the celebration was accorded by a unanimous vote of the Senate. Like his famous predecessor, Sir Isaac Newton, Sir George Stokes had been one of the University's representatives in Parliament, and he had devoted the whole of a long life to the prosecution of study and research within the University. There were, indeed, some remarkable points of resemblance in the careers of Sir Isaac Newton and Sir George Stokes. Both, at the time of their election to the professorship, were comparatively young men, both represented the University in Parliament, and both filled the office of President of the Royal Society.

"The proceedings in celebration of the jubilee extended over two days, June 1st and 2nd, 1899, and included on the first day the Rede Lecture, delivered by Professor Cornu, member of the French Institute, a conversazione, and a presentation to the University and to Pembroke College of busts of Sir George Stokes; while the programme of the second day included a reception of the guests of the

University and presentation of addresses, the presentation of an address from the University and of a commemorative gold medal to Sir George Stokes, the conferring of honorary degrees, a garden party at Pembroke College, and a dinner in the hall of Trinity College.

"These events were all arranged to do honour to a great son of the University; but perhaps the highest tribute to Sir George Stokes's merits, and their widespread acceptance, was to be found in the distinguished company of guests who had assembled to present the addresses sent by universities, academies, colleges, and learned societies in every quarter of the globe. To attempt to recite the names of the delegates thus assembled would be to enumerate those who, in the British Empire, on the Continent, and in America, have made themselves famous in the world of letters, science, and mathematics. In addition to the medal presented by the University, Sir George Stokes also received, at the hands of Professor Cornu, a medal granted to him by the French Institute, an unexpected honour which he deeply appreciated.

"Only in August last, on the death of Dr. Searle, Sir George Stokes agreed to be put in nomination for the Mastership of Pem'roke. He had long been the senior Fellow, and there is little doubt that he might, if he had wished, have been elected when Dr. Power died in 1880. But the recent vacancy came when the College had lost several of its most promising tutors, and Sir George agreed to accept the office. But he urged that at his time of life, eighty-three, he should not be put to the strain of changing his residence, and it was found that the Pembroke statutes contained a clause permitting the Master to reside elsewhere. He therefore continued to reside with his daughter and son-in-law, and the College had recently allowed the lodge to be used in part for University purposes.

"Sir George Stokes was married, in 1857, to Mary, daughter of the Rev. T. R. Robinson, D.D., Director of

Armagh Observatory. Lady Stokes died in 1899. From 1887 to 1892 he was one of the Members of Parliament for Cambridge University. In spite, or perhaps because of, his great and profound knowledge and remarkable ability, he rarely spoke in the House of Commons, but was always listened to with attention. In private life his simplicity and modesty were as conspicuous as his great attainments.

"During a period of forty years Sir George Stokes held the office of Churchwarden at St. Paul's Church. He was people's warden for one year, and vicar's warden for the remainder of the time. Always deeply interested in the events of the Church, he was a frequent attendant at the Vestry and other meetings. He read the lessons continuously for twelve years. After his appointment as Master of Pembroke he attended Chapel in the morning, but at the beginning of the vacation in December resumed the duty of reading the lessons at St. Paul's Church, and continued to do so until Christmas.

"It is merely true, though it may sound paradoxical, to say that there are men so great that their greatness is not readily demonstrable. Such a man was Sir George Gabriel Stokes. He presented the rare combination of extraordinary penetration with extraordinary breadth of intellect, producing a lucidity and completeness of treatment which masked difficulties he had surmounted.

"Stokes's characteristics as a teacher were lucidity and suggestiveness. He gave those who listened to him the impression of having his subject clear before him, and of having seen through it and beyond it to an extent not given to most men. Thus his work, both as a teacher and as a pioneer in more than one branch of physical mathematics, never appealed to the crowd, but was appreciated at its true value by those who were themselves in the front rank of scientific investigators. His chief laurels were won in the sphere of physical optics; but the remarkable breadth and penetration of his mind carried him, always with success, into subjects not less difficult,

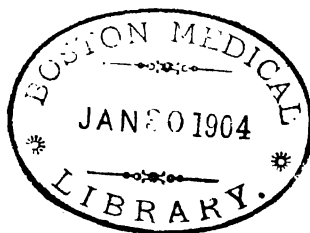
which in some cases had but a remote connection with his principal study."

A Fellow to whom I am indebted for the foregoing, adds:

"He was intensely interested in the treatment of lupus and other diseases by light rays and X rays, and used to come to Addenbrooke's Hospital to see the lupus lamp at work, and had hoped to have made some experiments in connection with it.

"His mental faculties were unimpaired to the last."





A NOTE  
ON THE  
CAUSATION AND TREATMENT OF THROMBOSIS  
OCCURRING IN  
CONNECTION WITH TYPHOID FEVER

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Received October 7th—Read November 25th, 1902

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WE have recently, in the hope of learning something of the causes of the thrombosis which is met with in connection with typhoid fever, addressed ourselves to the task of making a series of comparative observations on the blood in (a) typhoid fever patients in the acute stage

of the disease, (b) convalescents from typhoid fever, and (c) in normal persons. Led by considerations which will presently appear, we measured in each case the coagulation time of the blood and its content in lime salts.

As a preliminary, a word or two may be devoted to the methods employed.

### METHODS.

*Determination of coagulation time.*—The measurement of the coagulation time was in every case undertaken at half blood-heat, or at a temperature closely approximating to this. The capillary coagulation-tubes employed were made from ordinary glass tubing drawn out in the flame. They were calibrated by introducing into the wide upper end of the tube in each case 5 c.mm. of mercury, only those tubes being selected for use where this volume of mercury formed in the capillary stem a column exactly 5 cm. in length. In carrying out this calibration, the technique described by one of us in a recent number of the 'Lancet'<sup>1</sup> was followed. Some minor modifications were, however, introduced. The first of these was that, blowing out the tubes in the ordinary way over filter-paper, we adjudged coagulation to be complete as soon as a definite coagulum made its appearance, irrespectively of the fact that such a clot might not be adhering firmly to the walls of the capillary tube.<sup>2</sup>

Another modification which we introduced was that in our later observations—and these include all those undertaken upon normal men—we made it a practice to fill in our series of coagulation-tubes from a succession of slight pricks made as they were required, instead of from one deep prick made at the outset. In this way we altogether avoid the fallaciously accelerated coagulation which

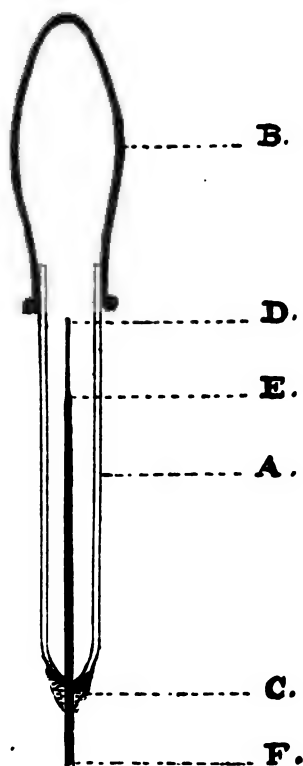
<sup>1</sup> July 5th, 1902.

<sup>2</sup> This modification in the procedure was dictated by the fact that where the coagulability of the blood is greatly reduced the coagulum may never become firm enough to block the tube.

is obtained from undue pressure on the finger and the occurrence of coagulation in the wound.

Lastly, we employed for the measurement of the standard volume of mercury, a special form of capillary

FIG. 1.



- A. Wall of the glass tube which forms the barrel of the pipette.
- B. Wall of the rubber teat.
- C. Sealing-wax luting the lower end of the tube. .
- D. Filiform open extremity of the inner measuring tube.
- E. Point at which the inner tube is restricted.
- F. Orifice of the inner measuring tube.

pipette which takes up from the reservoir in an automatic manner the exact quantity of mercury which is required for the calibration (Fig. 1).

This automatic pipette is made as follows:—Taking in hand a capillary pipette such as might serve for the estimation of blood coagulability, we fuse it near the point in the flame of a peep-light, draw it out here into an absolutely hair-fine tube, and break this across. A 5-c.mm. volume of mercury is now, as in the calibration procedure described above, introduced. This column of mercury is driven down the capillary stem, expelling the air in front of it, until it is definitely arrested by the narrowing of the lumen. By the fact of this arrest, the hair-fine tube approves itself to be for all practical purposes closed to mercury. Noting now the level of the proximal end of the mercury column, we mark this with a file, and here snap across the capillary stem, obtaining the measuring tube we require. We now break off from the mouth-piece of our original pipette what remains of the capillary stem, and invaginate into the butt-end thus obtained our capillary measuring tube. As shown in the figure, we dispose it so that its filiform extremity may be uppermost and entirely under cover of the outer tube. Finally, with sealing-wax we make an air-tight joint between the inner and outer tube. When the pipette is to be brought into use, it is furnished with a tightly-fitting rubber teat, air is expelled from the interior, and the distal extremity (F) of the inner (capillary) tube is brought below the surface of mercury. This last, under the influence of the negative pressure, will now run up until it is arrested at the point (E) before mentioned, where the lumen of the capillary tube is too narrow to admit mercury. By the aid of this simple automatic pipette any desired number of standard volumes of mercury may be measured out in an expeditious and accurate manner.

*Estimation of the content of the blood in calcium salts.*—The method outlined by one of us elsewhere<sup>1</sup> was employed. The essential feature of the method is the mixture in capillary tubes of a succession of progressive

<sup>1</sup> 'Transactions of the Pathological Society of London,' 1900, p. 304, and 'Lancet,' *loc. cit.*, 1902.

dilutions of a solution of neutral oxalate of ammonium, with, in each case, an equal volume of blood. The content in calcium salts—or, more strictly, the amount of calcium salts available for the purposes of blood coagulation—is appraised by noting the minimum concentration of ammonium oxalate required to keep the blood fluid. Coagulation is judged to have been averted when no trace of clotting appears in an oxalate tube within an hour after coagulation has taken place in the blood unmixed with oxalate.

The details of the procedure are as follows:—Starting from a solution of 1 in 500 of oxalate of ammonium in 0.75 per cent. salt<sup>1</sup> solution, a progressive series of dilutions are made, using normal salt solution as a diluent. The dilutions which will ordinarily be required in the case of human blood will be dilutions of 1 in 800 to 1 in 2000 or over.<sup>2</sup>

Having made our series of dilutions, we now place a small drop of each successive dilution—measured out in an uncalibrated capillary pipette—in series upon the surface of a microscope slide. This done, we fill into the same pipette from the patient's finger, a succession of precisely similar measures of his blood. We take, of course, for each successive oxalate solution a separate volume of blood, dividing off by a series of air bubbles. The required number of measures of blood obtained, we blow these out severally with a minimum of delay into the

<sup>1</sup> Chemically pure reagents must be employed.

<sup>2</sup> For the method of making exact dilutions in an uncalibrated capillary tube see Wright, 'Lancet,' July 5th, 1902 (introductory portion of paper, Section I). By the aid of the method there described, the dilutions employed in the observations incorporated in Table I were obtained as follows:—the 1 in 800 dilution by taking up into the capillary pipette 5 volumes of the 1 in 500 dilution and 3 volumes of diluting fluid; the 1 in 1000 dilution by mixing equal volumes of the 1 in 500 solution and of normal salt solution; the 1 in 1333 solution by taking 3 volumes of the 1 in 1000 solution and 1 volume of salt solution; the 1 in 2000 and 1 in 4000 dilutions by taking up in each case 1 volume of the 1 in 500 dilution, and in the one case 3 and in the other case 7 volumes of diluting fluid.

successive drops of oxalate solution, in each case mixing. Our pipette empty, we go over the whole succession of mixtures a second time to secure that mixture shall be quite complete.

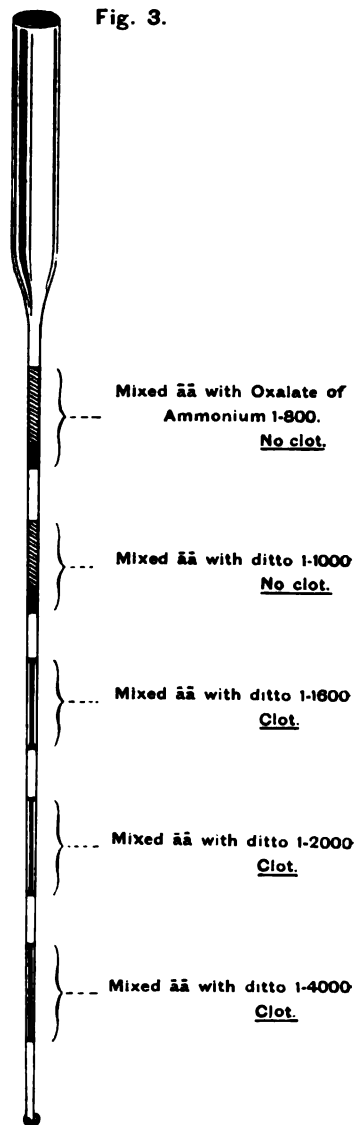
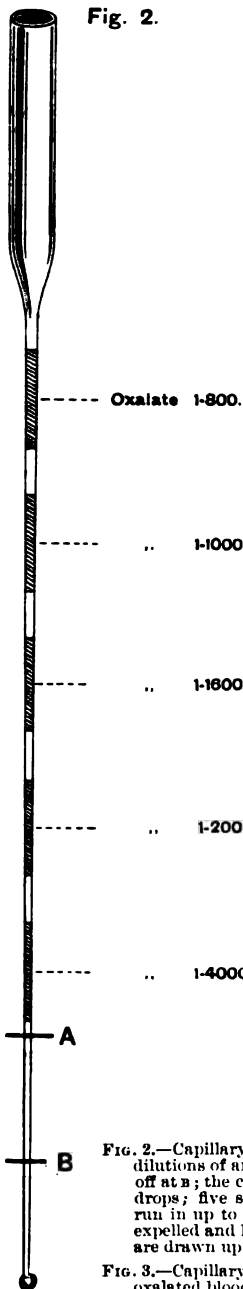
The final step in the procedure is to dispose of our oxalated bloods in such a manner as to observe their behaviour.

We may, if we please, fill them each into a separate capillary tube, and test their condition with respect to coagulation by blowing them out, after the expiration of the necessary interval, upon filter-paper.

Or—and this when practice has been acquired is more convenient—we may, dividing off as before by air bubbles, fill in, as shown in Fig. 3, the whole series of oxalated bloods into the capillary pipette which has served for the preliminary operations of measuring and mixing. If we follow this last procedure, we place the capillary pipette upright, and judge of the result after a sufficient interval, taking note whether the red blood-corpuscles have sedimented leaving a supernatant layer of plasma, or whether a filament of clot occupies the centre and a clear layer of serum has appeared along the walls of the tube.

For ward work it will be found convenient to bring to the bedside, instead of the series of watch-glasses containing the oxalate dilutions, a capillary pipette (sealed up after it has been drawn out into a hair-fine tube) filled in, as shown in Fig. 2, with a series of equal measures of the dilutions divided off by air bubbles. The pipette which does duty as a storage-tube for these dilutions will be available for the subsequent operations as described above if we take the precaution of marking off upon the capillary stem, before we empty it, a length (A—B in Fig. 2) corresponding to the particular volume of fluid which is to serve as our unit of measure.

Wright and Knapp: Causation and Treatment of Thrombosis.



**FIG. 2.**—Capillary pipette filled in with a series of equal volumes of progressive dilutions of ammonium oxalate. When brought into use the tube is broken off at *B*; the contained volumes of oxalate are expelled in a series of separate drops; five similar volumes of blood, measured by allowing the blood to run in up to the point *A*, are then filled in; lastly, after these have been expelled and have been mixed with the oxalate dilutions, the oxalated bloods are drawn up into the pipette, and the effect observed is as shown in Fig. 3.

**FIG. 3.**—Capillary pipette which has been filled in with a series of volumes of oxalated bloods, the dilutions being in each case as indicated in the figure.





## RESULTS OF THE BLOOD EXAMINATIONS.

*Results of the blood examinations undertaken on normal men.*—In Table I will be found arranged in tabular form the results of a series of blood examinations undertaken upon normal men. A consideration of these brings out the fact that there is as between different individuals, and, we may add, between the blood drawn off at different times from the same individual, a considerable difference not only with respect to the blood coagulation time, but also with respect to the content in lime salts. We find that the coagulation time, determined as explained above, may, in the normal male adult, vary between three and a half minutes and eleven minutes, and the minimum strength of oxalate of ammonium solution required to avert coagulation from 1 in 800—this being altogether exceptional—to 1 in 2000.

Of importance in connection with the method of measuring the content of the blood in lime salts is the fact that it comes out clearly in Table I, and will appear more clearly in the subsequent tables, that a blood which contains less calcium salts than a control blood is not always less coagulable; nor, again, is a blood which contains more lime salts necessarily more coagulable than the control. The content of a blood in lime salts as estimated by this method is, in fact, far from being an index of its coagulability.

*Results of the blood-examinations undertaken upon typhoid fever patients during the acute stage of the disease.*—These results are presented in Table II. The most noteworthy feature here is the general diminution of blood coagulability.<sup>1</sup> Let it be observed also that the diminished coagulability furnishes an explanation of the serious hæmorrhages which may occur from comparatively small lesions in the typhoid intestine. Exceptions to the pre-

<sup>1</sup> It may be remarked that a comparable diminution in the coagulability of the blood supervenes upon the inoculation of large doses of "anti-typhoid vaccine."

vailing rule of the association of a condition of diminished blood coagulability with the acute stage of typhoid fever are furnished by Cases 8, 9, and 10. The first of these was a very mild case. In the last, favoured no doubt by the pneumonia and bronchitis which were marked features in this case, femoral thrombosis developed in an acute manner. The symptoms had manifested themselves only a few hours before the blood was withdrawn for examination.

*Results of the blood examinations undertaken upon convalescents from typhoid fever.*—The results we have obtained are incorporated in Table III. The salient feature in connection with these results is the marked increase of blood coagulability which accompanies convalescence from typhoid fever. Taking the first eight cases—all cases which were examined both during the course of the pyrexia and after the return of the temperature to the normal,—we find that the coagulation time of the blood was, on the average, four and a half times shorter in the convalescent stage than during the course of the fever (four and a half minutes as compared with twenty minutes). In Cases 1, 4, and 14, and to these may be added Case 9 from Table II, blood coagulation was abnormally rapid. In each of these cases femoral thrombosis had supervened. And these were the only cases among those examined in which it had occurred. Somewhat exceptional, though not standing entirely by itself, is Case 13. Here the diminished coagulability, which has been shown to be a feature of the acute stage of the disease, is seen to have persisted into the convalescent period. On the thirteenth day after the return of the temperature to the normal, the blood coagulation time was found to be thirty-five minutes, and this in spite of the fact that the blood contained more than the normal quantum of lime salts. On the fortieth day the coagulation time was still somewhat prolonged.

Turning our attention now more particularly to the results of the calcium salt estimations, we see that the average content of the blood in lime salts, as estimated by

the oxalate method, is, in the case of these typhoid convalescents, about twice that of the normal blood.

*Therapeutical significance of the above facts.*—Limiting ourselves here to the consideration of the question of the therapeutics of thrombosis, we may, as a preliminary to setting forth the treatment we adopted, direct attention to a fundamental point in connection with intra-vascular coagulation. Arguing from what occurs *in vitro*, we might expect that in the case where a thrombus forms in a vein, the patency of the vessel would be rapidly restored by the contraction of the clot. We do, as a matter of fact, see this happening in connection with the intra-vascular thrombosis, which supervenes upon the injection of cell-nucleo-albumens (Wooldridge's "tissue fibrinogens"). If the animals survive this thrombosis for a few hours, we find the thrombus, which previously blocked the vessel, represented by a mere filament of clot. But the conditions are here quite special. As pointed out by Wooldridge, there supervenes here upon the "positive phase" of increased coagulability which culminates in the thrombosis a "negative phase" of diminished or abolished blood coagulability. By reason of the supervention of this "negative phase," the thrombus, when once formed, does not receive any further accretions of fibrin from the circulating blood.

Quite different are the circumstances when the blood maintains its original coagulability. Here, as soon as any blood-flow is re-established past the clot, additional fibrin will be deposited, and the thrombus will grow larger and firmer until at last it is converted into a solid plug of "white blood-clot," which definitely blocks the vessel. Probably in this way are sown the seeds of the permanent trouble so often seen after typhoid thrombosis, and we may add after phlegmasia alba dolens.

Recognising the practical importance of the after-deposition of fibrin upon the thrombus, the coagulation time of the patient's blood subsequent to the development of thrombosis is a matter of concern. A reference to Table III will show that in each of the cases of throm-

bosis—and these were examined respectively eight, twenty-one, and forty-five days after the date of the original thrombosis—the blood was found to be abnormally coagulable. The blood conditions were thus, at these dates, still favourable to a deposition of fibrin upon the clot.

We proposed to ourselves, both in these cases and in the case of acute thrombosis, referred to above as having occurred during the pyrexial stage of the fever, to place an obstacle in the way of this deposition of fibrin by diminishing the patient's blood coagulability. With this view we administered a decalcifying agent<sup>1</sup>—citric acid.

In Table IV will be found details of the amount of citric acid given, and of the effect of the treatment. It will be seen that in each of the seven patients observed the exhibition of citric acid was followed by a decalcification of the blood and a corresponding diminution of its coagulability. Hand-in-hand with the blood changes went, in the case of acute thrombosis already referred to, a rapid alleviation of the symptoms.

*Inferences with regard to the causation of the thrombosis which occurs in connection with typhoid fever.*—Turning, in conclusion, to the problem as to what is the cause of the thrombosis so frequently seen in connection with typhoid fever, and scrutinising the results of the blood examinations to see whether they shed any light upon this problem, our attention fastens on the fact that the quantum of lime salts in the blood of the typhoid convalescents examined was greatly in excess of that in the normal blood. This fact suggests that the increased coagulability during the convalescent stage may be dependent upon an excess of lime salts. Evidence pointing in the same direction is afforded by the circumstance that the blood coagulation times of our typhoid patients, after the con-

<sup>1</sup> For previous experiments on the effect of the exhibition of decalcifying agents (citric acid and soap) see Wright, 'British Medical Journal,' July 14th, 1894, and 'Transactions of the Pathological Society,' vol. li, part iii, 1900.

tent of their blood in lime salts had been brought within the limits of the normal, were (as is brought out by a comparative study of Tables IV and I) longer than those of normal bloods, instead of being shorter, as we should expect them to be if the increased coagulability were dependent upon an increase in the albuminous elements which enter into the composition of the fibrin.

When we consider whence the excess of lime salts which appears to be present in the blood of the typhoid convalescent can be derived, we recognise that it must be derived from the milk which, for the most part, constitutes the exclusive dietary of the patient. Cow's milk, be it noted, contains 1 part in 600 of CaO as compared with 1 part in 800 contained in lime water.<sup>1</sup>

If we have, in the milk dietary of the typhoid patient, the key to the problem of the frequency of thrombosis in the period of convalescence, we have probably obtained a clue also to the resolution of certain other problems; in particular the problem of the frequently beneficial effect of a milk dietary on "serous hæmorrhage" from the kidney, and the comparative rarity of thrombosis after acute fevers such as Malta fever, where a milk dietary is not imposed upon the patient.

We obtain at the same time indications for the prophylaxis and after-treatment of thrombosis, both when it occurs in connection with typhoid fever and when it occurs in connection with other diseases. The remedial measure which would seem indicated is the exhibition of citric acid. The same treatment, initiated as soon as the danger of intestinal hæmorrhage has been surmounted, would be appropriate for prophylaxis of typhoid thrombosis.

Or, as an alternative, we might, with a view to restricting the intake of lime salts, appropriately undertake a partial decalcification of the milk. One of us has already pointed out<sup>2</sup> that a partial decalcification such as is here con-

<sup>1</sup> In the case of our patients milk formed a very important element of their dietary for a period of many weeks after convalescence.

Wright, 'Lancet,' July 22nd, 1893.

templated is advisable also from the point of view of rendering the milk more easily digestible, and of preventing constipation. The partial decalcification in question can be readily effected by adding to the milk 0.25 to 0.5 per cent. of citrate of soda (20 to 40 grains per pint).

TABLE I.—*Normal Men.*

Showing the blood coagulation time and the strengths of neutral ammonium oxalate solution which respectively averted and failed to avert coagulation when added to the blood in equal volume.

Initials of the persons who furnished the blood.	Coagulation time, estimated in capillary tubes of the new standard size at 18°5° C. (half blood-heat).	Concentration of the solutions of oxalate of ammonium solution which were mixed with the blood for the purpose of estimating its content in calcium salts.					
		1 in 800 (5 in 4000).	1 in 1000 (4 in 4000).	1 in 1333 (3 in 4000).	1 in 1600 (2.5 in 4000).	1 in 2000 (3 in 4000).	1 in 4000 (1 in 4000).
A. W.	6' 30"	0	0	Trace	—	Clot	Clot
C. K.	7' 10"	0	0	"	—	"	"
E. C.	11'	0	0	Clot	—	"	"
G. E. V.	8' 15"	0	0	"	—	"	"
A. A.	7' 30"	0	0	0	—	"	"
S. D.	5' 45"	0	0	0	—	"	"
R. W.	6' 10"	0	0	0	—	"	"
J. S.	9' 15"	0	0	0	—	"	"
J. R.	8' 10"	0	0	0	—	"	"
B. S.	10' 15"	0	0	0	—	"	"
E. E. S.	9'	0	0	Trace	—	"	"
J. B.	10' 10"	0	0	Clot	—	"	"
O. N.	8'	0	0	"	—	"	"
W. B. L.	4'	0	0	Trace	—	"	"
G. E. V.	8' 45"	0	0	0	0	"	"
N. M.	8'	0	Clot	Clot	Clot	"	"
N. C.	6'	0	0	0	0	"	"
J. M.	8'	0	0	0	Clot	"	"
C. P.	9'	0	0	Trace	"	"	"
D. B.	6' 30"	0	0	Clot	"	"	"
W. E. <sup>1</sup>	8'	Clot	Clot	"	"	"	"
P. L.	7'	0	0	0	"	"	"
T. Y.	8' 20"	0	0	0	"	"	"
M. M. <sup>2</sup>	6'	0	0	0	"	"	"
M. M. <sup>2</sup>	3' 30"	Clot	Clot	Clot	"	"	"
W. E. <sup>1</sup>	6' 30"	"	"	"	"	"	"
T. H.	6'	0	0	"	"	"	"

<sup>1</sup> The observations here in question were made at an interval of a few days.

<sup>2</sup> The observations here in question were made at an interval of about forty-eight hours.

TABLE II.—*Typhoid Patients in the Acute Stage.*

Showing the results of the blood examinations undertaken on typhoid fever patients (soldiers) in the acute stage of the disease.

Serial number.	Notes with regard to the clinical features of the case and the stage of the disease at the date of the observation.	Coagulation time.	Estimation of content of blood in calcium salts, i. e. concentration of oxalate of ammonium solution, which (added to the blood in equal volume) just sufficed to avert coagulation.
Case 1	Fourth week of pyrexia; case has been complicated by epistaxis and pleural effusion	30'	1 in 2000
Case 2	Beginning of fourth week of pyrexia	12'	1 in 750
Case 3	Eleventh day of relapse	15'	1 in 900
Case 4	About seventeenth day of pyrexia	22'	1 in 2000
Case 5	Uncomplicated case; temperature falling by lysis	15'	1 in 2500
Case 6	About fourteenth day of pyrexia	30'	1 in 1500
Case 7	Tenth day of relapse	30'	1 in 900
Case 8	Tenth day; very mild case	5'	1 in 900
Case 9	Fourth week of pyrexia; complicated by pneumonia, capillary bronchitis, and on day of observation by acute femoral thrombosis	1' 45"	1 in 700
Case 10	Uncomplicated case; beginning of fourth week	5'	1 in 600
Case 11	Fourth day of relapse; history of hæmorrhages in primary attack	17'	1 in 1000
Case 12	Beginning of fourth week of pyrexia; much bronchitis	16'	1 in 900



TABLE III.

Showing the results of the blood examinations undertaken on soldiers convalescent from typhoid fever.

Serial number.	Notes with regard to the clinical features of the case and the stage of convalescence at which the patient had arrived at the date of the observation.	Coagulation time (followed in brackets by the coagulation time as previously determined in the stage of pyrexia).	Estimation of content of the blood in calcium salts, i. e. concentration of ammonium oxalate solution, which (added to the blood in equal volume) just sufficed to avert coagulation.
Case 1	Fourteenth day of apyrexia; three weeks subsequent to development of slight femoral thrombosis	2' [30']	1 in 900
Case 2	Twenty-fourth day of apyrexia	4' 15" [12']	1 in 700
Case 3	First day of apyrexia	4' 30" [15']	1 in 1500
Case 4	Seventh week of apyrexia; eight days after development of slight femoral thrombosis	1' 10" [22']	1 in 700
Case 5	Twentieth day of apyrexia; after taking citric acid 2.5 grammes t. i. d. for six days	4' [15']	1 in 1500
Case 6	Second day of apyrexia	4' [30']	1 in 700
Case 7	Seventh day of apyrexia	10' [30']	1 in 1500
Case 8	First day of apyrexia	5' [5']	—
Case 13	Thirteenth day of apyrexia	35'	1 in 700
Case 14	Fortieth day of apyrexia	11'	1 in 900
	Fifty-fifth day of apyrexia; forty-fifth day after development of thrombosis	1' 30"	1 in 700
Case 15	Third week of apyrexia	3' 15"	1 in 700
Case 16	Fourteenth week of apyrexia	9'	1 in 550
Case 17	Third week of apyrexia	9' 30"	1 in 700
Case 18	Third week of apyrexia	10'	1 in 800
Case 19	First day of apyrexia	7'	1 in 700
Case 20	Fifth day of apyrexia	4' 30"	—
Case 21	Fifth day of apyrexia	5'	—
Case 22	Tenth day of apyrexia	9' 30"	—

TABLE IV.  
Exhibiting the effect of the decalcifying treatment adopted in the case of typhoid convalescents possessing an unduly coagulable blood.

Initials of patient.	Date of observation.	Notes with regard to dietary and treatment.	Notes with regard to clinical symptoms at date of observation.	Blood coagulation time in standard tubes, at 15.5° C.	Estimation of content of blood in calcium salts. Concentration of ammonium oxalate solution which, when added in equal volume to the blood, respectively averted and failed to avert coagulation.			
					ago	ago	ago	ago
J. B.	8.7.02	Milk diet	Typhoid fever, fourth week, complicated by pneumonia and capillary bronchitis; today acute development of femoral thrombosis	1' 45"	0	0	Clot	Clot
	10.7.02	Ditto + citric acid 4 grms. (5j) t. i. d. (since 8.7.02)	Pain and swelling in limb less; fever continues	6'				
	11.7.02	Ditto	No change	7' 30"	0	0	"	"
	13.7.02	Ditto	Œdema and pain in the limb have quite disappeared; fever continues	7' 15"	0	0	"	"
	14.7.02	Ditto	No change	5' 45"	0	0	0	"
B. D.	7.7.02	Convalescent diet, including milk (circ. 2 pints)	Fourteenth day of pyrexia; twenty-second day after slight thrombosis	2'	0	0	Clot	Clot
	14.7.02	Ditto + citric acid 2.5 grms. (circ. 36 grs.) t. i. d. (since 12.7.02)	—	3' 45"	0	0	Trace	"
	19.7.02	Ditto	—	Over 15'	0	0	0	"

C. D.		Convalescent diet, including milk (circ. 2 pints) Ditto + citric acid 2.5 grms. t. i. d. (since 12.7.02) Ditto	Fifty-fifth day of apyrexia; forty-fifth day after thrombosis	1' 30"	0	Clot		Clot	Clot	Clot
						Trace	0			
J. A.	8.7.02	Convalescent diet, including milk (circ. 2 pints)	—	3' 15"	0	Trace	0	Clot	Clot	Clot
	14.7.02	Ditto + citric acid 2.5 grms. t. i. d. (since 12.7.02)	—	10'	0	0	0	Clot	Clot	Clot
	19.7.02	Ditto	—	1' 10"	0	Clot	Clot	Clot	Clot	Clot
	15.7.02	Convalescent diet, including milk (circ. 2 pints) Ditto + 2.5 grms. of citric acid t. i. d. (since 12.7.02)	Seventh week of apyrexia; seventh day after thrombosis	5'	Trace	Trace	Trace	Clot	Clot	Clot
D. R.	20.7.02	Ditto	—	Over 20'	0	0	0	Clot	Clot	Clot
	8.7.02	Convalescent diet, including milk (circ. 2 pints)	Third week of apyrexia	3' 15"	0	Clot	Clot	Clot	Clot	Clot
	15.7.02	Ditto + 2.5 grms. of citric acid t. i. d. (since 12.7.02)	—	4' 45"	0	0	0	Trace	Clot	Clot
	19.7.02	Ditto	—	13' 30"	0	0	0	Clot	Clot	Clot
R. D.	8.7.02	Convalescent diet, including milk (circ. 2 pints)	Fourteenth day of apyrexia	9'	Clot	Clot	Clot	Clot	Clot	Clot
	15.7.02	Ditto + citric acid 2.5 grms. t. i. d. (since 12.7.02)	—	9' 30"	0	0	0	Clot	Clot	Clot
	19.7.02	Ditto	—	10'	0	0	0	Clot	Clot	Clot
	8.7.02	Convalescent diet, including milk (circ. 2 pints)	Third week of apyrexia	9' 30"	0	Clot	Clot	Clot	Clot	Clot
F. D.	16.7.02	Ditto + citric acid 2.5 grms. t. i. d. (since 12.7.02)	—	Over 13' 30"	0	0	0	Clot	Clot	Clot
	19.7.02	Ditto	—	Over 30'	0	0	0	Clot	Clot	Clot

## DISCUSSION

Dr. WILLIAM HUNTER thought the explanation given of the thrombosis from the increase of lime salts in the blood was instructive. The deductions in regard to the amount of lime salts were also instructive. The administration of sodium citrate had been found practically useful in the treatment of febrile cases in the London Fever Hospital. It was well known that typhoid patients were too largely fed with milk. He asked if Professor Wright's observations could be extended to diphtheria treated by antitoxin.

Dr. H. D. ROLLESTON asked if Professor Wright considered that the phlebitis and secondary thrombosis were both due to increased coagulability of the blood. It was generally thought that the phlebitis depended on an infection of the vein wall with typhoid bacilli. He pointed out that the cases of typhoid in South Africa showed an excess of cases of thrombosis. This had been ascribed to the use of tinned meats by the late Dr. Washbourn, and to the over-exertion of the lower limbs in the constant trekking of the troops, by himself; but it was possible that tinned milk might contain an excess of lime salts, and thus further, on Professor Wright's theory, the tendency to coagulation.

Dr. NEWTON PITT also pointed out that micro-organisms had been found in the thrombi in typhoid cases, and also with phthisis. It was, however, a question whether they appeared before or after the thrombus had formed. He asked if the total excess of lime salts found in the blood of patients with thrombosis in typhoid did not exceed that supplied by the milk. Also in regard to thrombosis in other diseases—especially in influenza—in which no excess of milk was taken, how could this be ascribed to an excess of lime salts? Similarly in gouty thrombosis the milk theory would not hold. He asked also how Professor Wright would explain the absence of thrombosis in milk-fed infants. A point had been put forward in the paper, however, of extreme practical value.

Dr. CYRIL OGLE suggested that the treatment by citric acid might be attended by some danger of embolism if it were begun after the onset of thrombosis in a vein, since its effect apparently would be to prevent complete occlusion and arrest of blood-stream in the vessel, on the wall of which a parietal thrombus had already formed. He asked whether, in the cases quoted, any lung symptoms had developed, such as a slight attack of pleurisy. Such symptoms were often misinterpreted, and their origin in small venous embolisms overlooked.

Professor WRIGHT, in reply, said that he had not made any bacteriological observations on the thrombosed vessels; he had not had the opportunity. He thought bacteria might be one factor in the process. He was far from wishing to maintain that lime salts were the only factor in causing thrombosis; his position was that when there was an excess of lime salts in the blood a slight increase of its albuminous substance, or of the leucocytes, might occasion a thrombosis. In regard to children, it was not known whether they absorbed the whole of the lime that was taken in the milk, and, moreover, blood coagulability was low in children. As to influenza, other causes of blood coagulation, no doubt, came into play, such, possibly, as an excess of leucocytes. But the ordinary causes of excessive clotting were absent in typhoid fever; hence he maintained that in this disease the excess of lime salts was probably the principal factor. He had seen no evidence of embolism after the administration of citrate of soda; nor did he see reason to anticipate it. He considered that the large number of cases of thrombosis in South Africa might be due to the use of condensed milk, as, of course, bulk for bulk, it must be richer in lime salts than fresh milk. The amount of milk in the diet would far more than suffice to account for the surplus of lime circulating in the blood.



ON  
ACUTE CEREBRO-SPINAL MENINGITIS  
CAUSED BY THE  
DIPLOCOCCUS INTRACELLULARIS OF WEICHSELBAUM  
A CLINICAL STUDY

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ABSTRACT OF PAPER.

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DURING the year 1901 there were admitted to the wards of the London Hospital an unusually large number of cases presenting the clinical characteristics of acute cerebro-spinal meningitis ; in many of these the nature of the infecting organism was shown by the report of Dr. William Hunter, at that time assistant bacteriologist to the hospital.

Through the courtesy of the physicians under whose care the cases were placed I have been permitted to make use of the notes, and for this permission I have to record my best thanks.

In the progress of knowledge concerning an infective disease the earliest research must necessarily be directed towards the discovery of an organism present in association with a certain definite group of symptoms ; at a later stage, if more than one organism has been isolated from different cases not easily to be distinguished in their clinical course, it becomes necessary to reverse the process and to take one organism as the constant factor and thus define the symptom group associated with its presence. The present research is the result of an endeavour to apply this method in the investigation of the pathological results of infection by the diplococcus intracellularis.

Hunter and Nuthall explained in the 'Lancet' for June 1st, 1901, their reasons for supposing that the organism they isolated from the cases in the London Hospital was identical with the meningococcus of Weichselbaum. In the present research I have endeavoured in the first place to analyse the symptoms and signs produced by infection with this organism ; secondly, to discuss the pathological conditions underlying these symptoms ; and finally, to make a comparison of the results with previous descriptions of this and some other allied diseases.

It has not been thought necessary to differentiate between the cases infected by the two types mentioned by Hunter in his paper, seeing that he was satisfied as to their identity, and it was not possible to find any points



of difference in the clinical course or in the post-mortem appearances which seem to support the view that the two types were different species. If, however, other organisms were found present with the *diplococcus intracellularis*, the cases so infected have, for the purposes of the present investigation, been placed in a separate class.

In the absence of any trustworthy test for the presence of tuberculosis during life it has been necessary to assume that where recovery has taken place tuberculous infection was not present; this assumption seems justifiable when the clinical histories of cases undoubtedly tuberculous are compared with those of cases undoubtedly free from such infection. The Arloing-Courmont reaction has not been sought in any of the cases, chiefly because it did not seem that the test was sufficiently investigated to be considered pathognomonic.<sup>1</sup>

Cases which by post-mortem examination have been shown to be due to a mixed infection of the tubercle bacillus and the meningococcus have been considered separately; and many cases, from which for some reason it was impossible to obtain any cerebro-spinal fluid, have been set aside as useless in an inquiry of this nature.

In twenty-two cases presenting the clinical characteristics of meningitis, the bacteriological report renders it probable that the infection was pure and due to the *diplococcus intracellularis meningitidis*. Of these, twelve proved fatal, and in nine post-mortem examination proved the absence of tuberculosis; in the remaining three, of which a post-mortem examination was not possible, the clinical course seemed to exclude tuberculous infection. In nine cases, organisms other than the tubercle bacillus were present, as well as the *diplococcus intracellularis*; these cases are considered separately. Seven cases in which there was shown to be a mixed infection with a bacillus tuberculosis and the *diplococcus intracellularis meningitidis* are also reported.

<sup>1</sup> Horton Smith and Arnitt, 'Trans. Brit. Congress of Tuberculosis,' 1901.

TABLE I.—*Cases which died soon*

No.	Name and date.	Age.	Onset.	Duration and result.	Rigidities.	Kernig's sign.	Movements.
1	Kate A., April 4th, 1901	8 months	Fit and broncho-pneumonia	Died 3rd day	Neckrigid; legs rigid; no retraction of head	Not present	Strabismus; rhythmical up-and-down movements of eyes
2	Sarah H., February 19th, 1901	7 years	Headache; restlessness; vomited once	Died 10th day	Retraction of head; legs flaccid	Present	Intermittent strabismus; twitching of face and right arm
3	Harry G., April 29th, 1901	7 years	Apathy; cough; fits with cyanosis	Died 8th day	Retraction of head	Present	Fits, generally right-sided
4	Joseph B., April 18th, 1901	4 years	Convulsions; screaming	Died 4th day	Retraction of head	Marked	Convulsions before admission
5	Deborah G., April 20th, 1901	2 years	Cough; no vomiting; no fits	Died 5th day	Neckrigid; head not retracted	Not present	Continuous movement of right arm and right side of face; strabismus
6	Alfred C., May 26th, 1901	32 years	Right pleurisy; delirium	Died 7th day	Neckrigid; head not retracted	Present	—
7	Alfred L., April 7th, 1901	19 years	Pain in head; semi-coma	Died 12th day	Neck rigid	Present	Slight strabismus

*after the onset of the disease.*

Vomit.	Fundi.	Temperature.	Bacteriology.	Meningitis.			Hydrocephalus.	Remarks.
				Vertical.	Basal.	Spinal.		
—	—	100.5°—105°	Diplococcus meningitidis in pure culture	Patches of lymph	A little lymph	Flakes of lymph	Some excess of fluid.	
At onset only	Veins full, otherwise normal	103°—105°	Ditto	Patches of lymph; vessels congested	Purulent lymph at base	Purulent lymph all down cord	Slight excess of fluid.	
Present	? Slight neuritis	100°—103°	Ditto	—	No post-mortem.			
—	Normal	102°—104.6°	Ditto	Lymph extending up from base	Purulent lymph	Lymph on cord, chiefly in lumbar region.		
—	—	102.4°—104.6°	Ditto	Purulent lymph extending from base	Purulent lymph; excess of fluid	—	No excess of fluid	Patches of broncho-pneumonia.
—	Normal	100.98°—105°	Ditto	Membranes milky	Excess of fluid	Membranes milky; no lymph	Excess of fluid	Old and recent pleurisy.
Once	Normal	100.98°—101°	Ditto	Congested lymph on frontal lobes	Lymph on superior of cerebellum	Lymph on cord.		

TABLE II.—*Cases which*

No.	Name and date.	Age.	Onset.	Duration and result.	Rigidities.	Kernig's sign.	Movements.
8	Henry R., March 27th, 1901	35 years	Severe head-ache; resembled enteric	Six months; death	Neckrigid; head retracted	Doubtful	Convulsions and strabismus towards the end
9	Fanny S., February 14th, 1901	2½ years	Vomiting; wasting	3½ months; death	Neckrigid; limbs rigid at times	Present	Nystagmus; dissociated movements of eyes; retraction of lids
10	May P., April 13th, 1901	8 months	Sudden cyanosis; retraction of head	7 weeks; death	Head retracted	Indefinite	Slow irregular movement of limbs; nystagmus; ocular squint; retraction of lids
11	Herbert C., July 19th, 1901	5 years	Diarrhoea and vomiting; head-ache; measles 3 weeks previously	7 weeks; death	Slight rigidity of neck	Present	R. pupil > L.
12	Winifred H., July 20th, 1901	3 years	Vomiting; head-retraction followed measles	5 weeks; death	Marked rigidity of neck; legs drawn up	Absent	No strabismus; no retraction of upper lids

*died later in the disease.*

Vomit.	Fund.	Temperature.	Bacteriology.	Meningitis.			Hydrocephalus.	Remarks.
				Vertical.	Basal.	Spinal.		
Attacks of vomiting lasting 3-5 days	Normal	Slight pyrexia for 2 weeks at onset	Diplococcus meningitidis isolated	Convulsions flattened; hemorrhage into pia mater	Excess of lymph	—	Large quantity of clear fluid	
Frequent	Normal	Normal and sub-normal	Ditto	Convulsions flattened; lobes adherent; no lymph	Excess of fluid	Some lymph or lumbar enlargement		
Present towards end	Normal	Normal	Ditto	Convulsions flattened; pia arachnoid congested	—	Excess of fluid in subarachnoid space; pia congestion	Ventricles distended; flocculent yellow material in ventricles	
Before admission	Normal	101°—normal	Ditto	—	—	No post-mortem		
At first	—	104°-99°	Ditto	—	—	No post-mortem		

TABLE III.—*Cases*

No.	Name and date.	Age.	Onset.	Duration and result.	Rigidities.
13	William H., March 24th, 1901	1½ years	Irritability	10 weeks; recovery	Occasional retraction of head
14	Dorothy R., April 1st, 1901	8 weeks	Increasing size of head	12 weeks; improved	Rigidity of neck and limbs (late)
15	Solomon B., April 4th, 1901	6 months	Broncho-pneumonia; convulsions	3½ months; hydrocephalus; improved	Retraction of head; opisthotonos; limbs rigid
16	Esther S., May 3rd, 1901	3 months	Constipation; convulsions; onset gradual	2½ months; recovery	Retraction of head; arms rigid
17	Ellen T., March 12th, 1901	3 months	Wasting; cough; convulsions; vomiting	5 months; recovery	Rigidity of neck
18	Esther L., April 20th, 1901	6 months	Feverish; vomiting; retraction of head	3½ months; improved	Retraction of head
19	George P., June 8th, 1901	5 years	Staggering gait	6 months; recovery	No rigidities
20	John E., July 6th, 1901	1½ years	Diarrhoea and vomiting; bronchitis	2½ months; recovery	Retraction of head
21	Albert P., August 5th, 1901	3 years	Vomiting; screaming	10 weeks	Marked retraction of head
22	John C., October 13th, 1901	3 years	Irritable	10 weeks	Retraction of head

*which recovered.*

Kernig's sign.	Movements.	Vomiting.	Fundi.	Temperature.	Bacteriology.
Present	Restless movements of head and eyes	Occasional	—	98°—104°	Diplococcus intracellularis found.
Present (late)	Strabismus; retraction of upper eyelids	Late	—	Normal	Ditto.
Present	Strabismus; retraction of lids	Occasional	Normal	Normal	Ditto.
Indefinite	No retraction of upper lids; no strabismus	Occasional	Normal	Normal generally; irregular rises	Ditto.
Present	Convulsions 1 week before admission; retraction of upper lids marked	Occasional	Normal	Normal	Ditto.
Not obtained	Occasional retraction of lids; dissociated movements of eyes	Present	Normal	Normal; occasionally rose to 102°	Ditto.
Not obtained	Internal strabismus; nystagmus	Present	Early neuritis	Normal	Ditto.
Not obtained	No strabismus	—	Normal	100°—normal	Ditto.
Present	Intermittent strabismus	Present	Normal	Irregular	Ditto.
Not obtained	Dissociated movements of eyeballs	Present	—	Normal	Ditto.

TABLE IV.—*Cases of single infection, Nos. 1—22.*

Age.	Group 1.	Group 2.	Group 3.	Total.
	Which died early.	Which died later.	Which recovered.	
1 year and under	2	1	2 months and under, 1 } 3 " " 2 } 6 " " 2 }	8
Under 2 years and over 1 year	1	0	2	3
" 3 " " 2 yrs.	0	2	2	4
" 5 " " 4 "	0	1	1	2
" 7 " " 5 "	2	0	0	2
" 19 " "	1	0	0	1
" 32 " "	1	0	0	1
" 35 " "	0	1	0	1
Total number of cases	7	5	10	22
Duration	Minimum 3 days; maximum 12 days; average 7 days	Minimum 5 weeks; maximum 6 months	Minimum 10 weeks; maximum 6 months	
Rigidity of neck	7	5	9	21
Retraction of head	3	0	8	11
Vomiting	Frequent, 1 case; once only, 2; no vomit, 3; no mention, 1	5	10	
Kernig's sign	5	3	5	13
Squint or dissociated movements of eyes	4	0	7	
Retraction of upper lids	0	2	3	
Temperature	Pyrexia, 100°—103°	Pyrexia at first, normal later, 4; pyrexia throughout, 1	Generally normal with irregular rises	
MORBID ANATOMY.				
Purulent meningitis	5 cases out of 6 post-mortems	1 case out of 3 post-mortems		
Ventricles distended with fluid	1 case out of 6	3 cases out of 3		



In all cases the bacteriological report was based upon the result of the system of examination detailed by Dr. Hunter in his paper. If there was evidence of contamination the case was excluded, so that so far as possible fallacies should be avoided.

*Cases in which the Meningitis in all probability was due to a single infection by the Diplococcus intracellularis meningitidis.*

*Age.*—Of the twenty-two cases collected, the ages varied from two months to thirty-five years. Eight were twelve months old or younger; three were between one and two years old; four between two and three; two were five years old; two seven years old; and the others nineteen, thirty-two, and thirty-five years respectively.

The condition, therefore, though occurring with greater frequency in early life, is not exclusively confined to that period. The question of age incidence is of importance in determining the relationship of this disease to posterior basic meningitis, and will be discussed later.

*Source of the infection.*—It has not been possible in these cases to trace the mode of infection. No instance has occurred in which there was any suspicion of transmission from person to person. In only one instance were two members of the same family similarly affected; this was in the case of Albert P— (No. 21), whose sister had been treated for posterior basic meningitis, at Great Ormond Street, in 1893.

No instance was met with in which two cases came from the same house; the homes of the parents were scattered widely through the East End of London, and in some instances the cases had been brought up from the country. There seemed nothing, in fact, to suggest that the disease was transmitted by contagion.

Where babies at the breast, hand-fed infants, children of older years, and adults seem indiscriminately affected,

it is at least improbable that the germ is introduced through the food or drink.

Bronchitic signs are not uncommon at the onset, but evidence of pulmonary disease is not invariably present. A nasal discharge is not so common as might be expected if the nose is the part through which the infection is introduced. In fact, so far as these cases are concerned, no evidence has been gathered which points conclusively to the mode of infection or to the manner of spread of the disease.

*Symptoms.*—When the cases are grouped together they seem naturally to fall into subdivisions, which present both clinically and pathologically definite points of difference.

Thus, to take the fatal cases, seven died in from three to twelve days from the onset of the disease, and it appears reasonable to suppose both on clinical and pathological grounds that death resulted from the severity of the meningitis. In five cases death occurred in from five weeks to six months from the commencement, and for many reasons the supposition seems justifiable that the fatal event was determined not by the actual meningitis, but by conditions consequent upon it. Closely allied with this second group of cases are those which terminated in recovery either partial or complete.

In discussing the symptoms, therefore, it is necessary to distinguish so far as is possible between those which are indicative of actual meningitis and those indicative of secondary conditions, of which the most frequent and most important are the excess of cerebro-spinal fluid and the distension of the cerebral ventricles.

*Onset.*—Of the seven cases which died early in the disease, three showed evidence of pulmonary disease when first seen; two seemed at first to be cases of bronchopneumonia; the third commenced with the symptoms and signs of a dry pleurisy. Of the other four, two began with severe headache, one with convulsions, one with incontinence of urine followed two days later by a succes-

sion of fits. Of the five cases which died later in the disease, in two the first sign of meningitis was headache occurring two or three weeks after an attack of measles, in one the onset was sudden, with what the mother described as "inward fits," and in the two remaining the onset was gradual, in one case resembling the onset of enteric fever, and in the other with vomiting and wasting. Of the ten cases which recovered, in five the onset was gradual, and it was not possible to fix closely the date when the illness first commenced; in three, convulsions ushered in the disease, in one irritability and anorexia were the first symptoms suggesting departure from health, and one began with diarrhœa, vomiting, and some bronchitis.

From a consideration of these points it seems clear that the development of symptoms and signs may in some cases be extremely gradual, though in the majority the ingravescence of symptoms is rapid as soon as the disease starts. In one case, Dorothy R— (No. 14), the disease had obviously progressed far, as evidenced by the enlargement of the head, before any symptoms were developed. As a general rule, however, the rapid development of symptoms and signs shows a considerable difference from the insidious onset of tuberculous meningitis, and is, therefore, of diagnostic importance.

Pulmonary disease somewhat frequently, but not invariably, precedes the symptoms of meningitis; when the frequency of bronchitis and broncho-pneumonia amongst East End children is considered, it is dangerous to lay much stress on pulmonary complications when considering the etiology of meningitis.

*Rigidity of the neck.*—The most marked sign, and that which most frequently first suggested the diagnosis of meningitis, was the rigidity of the neck, or rather resistance to forward flexion of the head. In one case only (George P—, Case 19) out of the twenty-two investigated was this sign absent, and he had been ill for four or five months before admission to the hospital.

In many cases there was very marked retraction of the head, producing the condition of cervical opisthotonos; but in others the rigidity, though marked, was not associated with much retraction. As a rule there was no resistance to rotation of the head, and difficulty in movement was only encountered when forward flexion was attempted.

Spinal opisthotonos was not marked in any of these cases; most frequently the patient lay upon the side with full flexion of the spine, even when the head retraction was so marked that the occiput seemed to lie between the scapulæ. In other cases that I have seen since, spinal opisthotonos was extreme.

In the cases that recovered, the rigidity of the neck, though it might vary from day to day, was usually one of the last signs to disappear.

*Kernig's sign.*—In the investigation of this sign of spinal meningitis, certain fallacies are likely to creep in which are very difficult to exclude. In the original description the sign is demonstrated by bringing the patient to the sitting posture and then attempting to straighten the knees. In a modified form, described by Professor Osler in the Cavendish Lecture, the patient remains in the dorsal decubitus; both hips are then flexed to a right angle with the trunk, and an attempt made to fully extend the knees. In well-marked cases the resistance of the hamstrings is so great that extension of the knees beyond a right angle is impossible. Osler's modification is advantageous in so far as it disturbs the patient but little.

In the less marked cases, however, with this method a fallacy may be introduced from tilting of the pelvis and flexion of the lumbar spine: the knees may be fully extended, but the flexion of the hips has been decreased so that no increase of tension is brought to bear upon the hamstrings.

To avoid this fallacy it is necessary to keep one hip fully extended, while the other is kept flexed to a right

angle, and the knee-joint is gradually extended. In this way the sign may be elicited without greatly disturbing the patient. Further, the presence of the sign, especially in adults, cannot be considered as pathognomonic of spinal meningitis. In cases of true sciatica, for instance, it can be very readily demonstrated, and in many perfectly healthy individuals full extension of the knee-joints, when the hips are flexed to a right angle, is a distinctly uncomfortable, if not impossible proceeding. Not many adults can perform the schoolboy trick of touching their toes without bending the knees. Sailer, too, has shown that it may occur in one leg in cases of focal brain disease.<sup>1</sup>

The question also arises concerning the degree of limitation in extension necessary before the sign can be said to be definitely present.

For the present purpose a rough limit of one and a half right angles has been taken. If, when the hip is flexed to a right angle and the other hip is fully extended, extension of the knee-joint can be effected beyond  $135^{\circ}$ , it has been taken that Kernig's sign was not definitely present.

The value of the sign seems to be somewhat doubtful; it does not seem possible to assert that the presence of this sign will establish the diagnosis of a case in which the other signs are equivocal. In five out of the seven cases that died in the acute stage of the disease the sign was present; in two it was definitely stated to be absent. In three out of the five which died later it was also present, and in five out of the ten that recovered it was obtained. In some cases it seemed to be variable, being only obtained occasionally.

*Mental disturbance.*—In those patients old enough to permit observations on this point an early and profound disturbance of the mental state was noticed. Sometimes at first there was very marked irritability and great resentment against any disturbance; this in the acute cases generally passed into a condition of drowsiness or semi-

<sup>1</sup> Sailer, 'Amer. Journ. Med. Science,' May, 1902.

coma, in which the patient took no notice of any interference, and, later, into a more profound coma preceding death. In those cases in which the clinical course was protracted the progressive mental deterioration could be more closely observed, and in those that recovered the inverse sequence of semi-coma, irritability, and "impaired cerebration" was often noticed.

There are probably two ways in which the functions of the brain may be disturbed in cases of meningitis. Early in the disease, associated with the meningitis there is a degree of inflammation of the cortex which gives origin to the rapidly developing coma. In this respect simple meningitis differs from the tuberculous form in which the mental faculties may be preserved until a comparatively late period of the disease. At a later stage of the disease, if hydrocephalus ensues, the brain functions may be mechanically disturbed by the increase of intra-cranial pressure. Sometimes there may even be a period of lull, or perhaps amelioration of symptoms, denoting the subsidence of inflammation, and prior to the development of hydrocephalus.

Either of these conditions, if the case be not fatal, may leave some degree of mental defect as a permanent legacy.

*Movements.*—At all stages of the disease it is common to find evidences of disturbance of the motor side of the nervous system. In young children convulsions may occur at the onset, in older patients they may only be an expression of some secondary complication, but in one case (Harry G—, No. 3) right side epileptiform fits were a prominent feature from the onset. From the commencement, dissociated movements of the eyeballs or an intermittent strabismus, in some cases producing a coarse kind of nystagmus, are not infrequently found. A permanent strabismus suggestive of nerve paralysis appears to be rare. In four out of the seven acute cases a squint was noticed; in one there was continuous rhythmic up-and-down movement of the eyes. Uncontrolled move-

ments of a monoplegic or hemiplegic distribution were noticed in two of the seven acute cases.

Later in the disease, and possibly associated with the supervention of internal hydrocephalus, it is common to find intermittent retraction of the upper eyelids, so that a line of sclerotic is shown above the cornea. This has been described as comparable to Stellwag's sign in Graves' disease, but it is not associated with any exophthalmos.

Epileptiform convulsions also may occur in the later stages of the chronic form, and probably are to be associated with the hydrocephalus rather than with the meningitis.

*Temperature.*—In the acute cases and at the onset, the temperature was generally raised, varying between 100° and 105°. Occasionally the temperature became very high just before death. In the chronic cases that were admitted shortly after the onset of the disease some irregular pyrexia was generally noticed at first, but later the temperature continued normal or subnormal. Sometimes, especially in young children, the temperature became markedly irregular in later stages when the intra-cranial pressure was high. The temperature chart differs as a rule from that of a case of tuberculous meningitis in so far as there is considerable pyrexia at the onset and during the first week or ten days, and then frequently a long apyrexial period. In tuberculous meningitis, on the other hand, the temperature is generally only slightly raised at first, and then in a more uniform manner.

*Wasting.*—Loss of flesh was a very marked feature in all cases, and seemed to be much more rapid than is usual in cases of tuberculous meningitis.

*Vomiting.*—In the acute cases vomiting was infrequent; in one only out of the seven cases did the vomiting become at all urgent. Two vomited once; the remaining four did not vomit at all.

On the other hand, in the more protracted cases,  
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whether they ended in death or recovery, vomiting became a marked feature as the disease progressed. The operation of lumbar puncture seemed not infrequently to have an immediately beneficial effect in checking this symptom. The necessary deduction seems to be that the vomiting is due rather to a rise of intra-cranial pressure than to the actual meningitis.

*Action of the bowel.*—In the majority of the cases, whether of the acute or chronic type, there was no tendency to constipation. Frequently actual looseness of the bowels was observed. In one case only out of the twenty-two (H. W. R—, No. 8) was there marked constipation, and this was the case that had a history of six months' illness before admission to the hospital. This point, though apparently unimportant, may serve at times in assisting the differentiation of this disease from tuberculous meningitis.

*Pulse.*—No special peculiarity has been noticed with regard to the pulse; in the acute stages the frequency was increased, but the phases met with in tuberculous meningitis were not observed. With the rise of intra-cranial pressure that appears to occur in the protracted cases, it seemed reasonable to expect a marked reduction in the pulse rate. This, however, has not been found. Irregularity of the rhythm was noticed, sometimes associated with marked severity of the other symptoms.

*Respiration.*—As a rule there was no marked alteration in the respiratory rhythm. Towards the end, in some of the bad cases, a grouped or periodic rhythm was noticed.

*Fundi.*—In twenty out of the twenty-two cases no alterations in the fundi were noticed. In one of the acute cases it was thought that there might be some early optic neuritis, but the observation was considered doubtful. In one of the cases that recovered a condition was found which was stated definitely to be early optic neuritis.

The changes in the disc described by Thursfield,



'Lancet,' February 16th, 1901, as occurring in posterior basic meningitis, though sought for, were not observed in any of the cases.

Blindness was apparently present in some of the cases without recognisable changes in the fundi; this disappeared later as convalescence was established.

Observations upon vision are extremely difficult to make when a patient is seriously ill, and consequently no extended research upon this point could be made.

*Hearing.*—In some of the cases, at certain periods of the disease, deafness seemed to be present, though in none was it permanent. Sometimes the attention of the patient could be attracted by sight where sounds seemed to produce no effect. Taste and smell could not be investigated.

*Hydrocephalus.*—In two cases in which the onset of the disease occurred before the synostosis of the cranial bones, definite enlargement of the skull was noted (Dorothy R—, No. 14, and Solomon B—, No. 15; and H. W. P—, Appendix II). In other cases the increase of fluid in the cerebral ventricles could only be surmised during life from the presence of certain symptoms which have already been discussed.

Bulging of the fontanelle, if still unclosed, was present in several of the cases, and seemed to be an indication of internal hydrocephalus. The bulging was generally relieved if a successful lumbar puncture was performed, *e. g.* Solomon B—, No. 15.

*Morbid anatomy.*—Of the acute cases, all save one (Alfred C—, No. 6) showed diffuse purulent leptomeningitis of brain and cord; the greatest collection of lymph was usually at the base, but there was, in all these cases, scattered lymph upon the vertex and down the spinal cord. In the single exception there was an excess of fluid in the ventricles and a milkiness of the membranes, but no definite lymph. In this group of cases the ventricles, though containing an excess of fluid, did not appear so distended as in those cases in which the disease ran a more protracted course.

TABLE V.—*Cases of*

No.	Name and date.	Age.	Onset.	Duration and result.	Rigidities.	Kernig's sign.	Movements.	Vomiting.
23	Elizabeth S., March 8th, 1901	6	Fell down- stairs; headache; vomiting began 5 days later	13 days; death	Rigidity of neck	Present	Fit; irregu- lar move- ments left hand; nys- tagmus; dis- sociated movements of eyes	At onset only
24	Bella C., March 11th, 1901	1 month	Convul- sions	2 days; death	Rigidity of neck	No note	Continuous convulsions	No note
25	Michael G., April 4th, 1901	4 months	Fits	8 days; death	Rigidity of neck (late)	Not ob- tained	Repeated convulsions	Nil
26	Samuel G., April 2nd, 1901	15 years	Headache	25 days; death	Rigidity of neck	—	—	Nil
27	Isaac M., May 7th, 1901	19 years	Sudden on- set; drow- siness; headache; vomiting; diarrhoea	8 days; death	Neck rigid; slight re- traction of head	Present later	Delirious; restless at first, stupor later; inter- mittent strab- ismus	Occa- sional
28	Jessie B., May 7th, 1901	1½ years	Sudden on- set with fit	25 days; death	Retraction of head	Not ob- tained	Frequent yawning; no squint; no retraction	At end frequent
29	Abraham D., January 30th, 1901	2 years 10 months	Irritable attacks of cramp; fits; wasting	3 months; death	Retraction of head marked	Not ob- tained	Strabismus; occasional retraction of upper lids	Fre- quent
30	Edwin T. R., March 2nd, 1901	4½ months	Convul- sions	4 months; death	Retraction of head marked	Not ob- tained	Occasional retraction of upper lids; no strabis- mus	Only during last week
31	Harry K., February 28th, 1901	1 year	Vomiting; fever; broncho- pneumonia	About 6 months; recovery	Retraction of head marked	Present	Strabismus; movements of lower jaw; later occa- sional retrac- tion of upper lids	3rd and 6th weeks frequent

*mixed infection.*

Fundi.	Temperature.	Bacteriology.	Meningitis.			Hydrocephalus.	Remarks.
			Vertical.	Basal.	Spinal.		
No definite changes	99°—101°; 102.4° just before death	Diplococcus intracellularis and pyogenic organisms	No lymph	Lymph at base and on cerebellum	Lymph down cord	Excess of fluid in ventricles at base and in spinal theca	Tubercle of the pericardium by direct extension was found, but apparently had not caused death.
—	100.4°	Ditto	Purulent meningitis.				
—	100°	Ditto	No evidence of meningitis	—	—	No excess of fluid.	
Normal	99.4°	Ditto	Convolutions flattened; no lymph	Much fluid; no lymph	—	Ventricles distended	Otorrhœa 5 years, ceased just before onset of symptoms; no mastoid signs.
Normal; ? blind; ? deaf	99°—130°	Diplococcus intracellularis and pneumococcus	Streaks of lymph	Lymph on under surface of cerebellum	Lymph all down cord	No excess of fluid; lymph in 4th ventricle	Developed signs of left basal pneumonia; post mortem, double apical and left basal pneumonia.
Both discs blurred	100°—103°, irregular, sustained	Ditto	No lymph	Purulent basal meningitis	Spinal meningitis purulent	No excess of fluid in ventricles	Signs of general broncho-pneumonia; post mortem, general broncho-pneumonia.
Optic neuritis	Normal	Diplococcus intracellularis and bacillus influenzae	No signs of meningitis; convolutions flattened	No sign of meningitis; membranes at base turbid	—	Ventricles enormously distended.	
Normal	Normal	Ditto	No signs of meningitis; convolutions flattened	Milkiness of membranes; no lymph	Much fluid in theca; no lymph	Ventricles enormously distended	Improved slightly for some time; diarrhœa and vomiting for last week before death.
Apparently blind for some time; normal	Irregular for 3 weeks, 97°—104.2°; later normal with occasional rise	Ditto.					

TABLE VI.—*Cases of mixed infection, Nos. 23—31.*

Age.	GROUP 1.	GROUP 2.	GROUP 3.	Total.
	Which died early.	Which died later.	Which recovered.	
1 year and under . . . . .	2 (1, 1 month; 2, 4 months)	1 (4½ months)	1	4
Under 2 years and over 1 year	1	0	0	1
„ 3 „ „ 2 yrs.	0	1	0	1
6 „ . . . . .	1	0	0	1
15 „ . . . . .	1	0	0	1
19 „ . . . . .	1	0	0	1
Total number of cases . . . . .	6	2	1	9
Duration . . . . .	Minimum, 2 days; maximum, 25 days; average, 13½ days	1, 3 months; 2, 4 months	6 months.	
Rigidity of neck . . . . .	6	2	1	9
Retraction of head . . . . .	2	2	1	5
Vomiting . . . . .	3 slightly	2 towards end	1 (3rd—6th week)	6
Kernig's sign . . . . .	2	0	1	3
Squint or dissociated move- ments of eyes . . . . .	2			
Retraction of upper lids . . . . .	—	2	1	3
Temperature . . . . .	Pyrexia	Normal	Irregular first 3 weeks; normal later.	
Purulent meningitis . . . . .	4 cases (6 post- mortems)	0 (2 post- mortems).		
Ventricles distended with fluid	2	2		

Post-mortem examination was only permitted in three out of the five cases which died at a later stage of the disease.

In these three cases the characteristic feature was the distension of the ventricles and the flattening of the convolutions. In all three a little yellow lymph was found in the descending horn of the lateral ventricles, floating in clear fluid. In one there was some lymph at the base of the brain; in another, some lymph found only on the cord most marked at the lumbar enlargement. In the third no lymph was found upon the meninges, but only some matting together of the convolutions.

*Cases in which there was a Mixed Infection.*

In four cases cultures from the cerebro-spinal fluid were found to contain the diplococcus intracellularis together with pyogenic organisms.

In two it was accompanied by the pneumococcus, and in three by a short bacillus resembling the bacillus influenzae.

In those cases where pyogenic organisms or the pneumococcus were present the clinical course corresponded to the acute type of pure meningococcus infection, death occurring between the second and the twenty-fifth day.

In one case (Michael G—, No. 25) there was no evidence of meningitis at the post-mortem examination, and in another (No. 26) there was only hydrocephalus without apparent meningitis; in the other three the appearances were those of acute leptomeningitis.

In the three cases in which the Bacillus influenzae was present the course was much more protracted; two died at the end of three and four months respectively, with post-mortem appearances suggestive of hydrocephalus as the cause of death.

The third (Harry K—, No. 31), though at one time showing signs suggestive of a marked rise in the intra-

cranial pressure, after six months made an apparently complete recovery.

The analysis of the symptoms points to the close relationship of this group with those where the infection was shown to be pure.

Rigidity of the neck is constant and appears early. In some there is definite retraction of the head ; in all cases there is impairment of the cerebral functions, though in the younger patients it is impossible to distinguish this from the peevishness very generally associated with ill-health. Kernig's sign is not constant. Occasionally dissociated movements of the eyes are found, producing an intermittent squint or even a coarse nystagmus. At the onset the temperature is usually raised, but as a rule to no great height. With the onset of internal hydrocephalus, vomiting and retraction of the upper lids are signs that become prominent.

*Cases infected by Bacillus tuberculosis and Diplococcus intracellularis.*

In six cases, the cerebro-spinal fluid of which during life was reported to contain the diplococcus intracellularis, acute miliary tuberculosis was found present at the autopsy.

In these the clinical course seemed to be somewhat longer than in the simple acute cases ; the average duration from the onset was twenty days, but none lived longer than twenty-six days.

Rigidity of the neck was a constant phenomenon, and dissociated movements of the eyeballs were noted in five out of six.

Pyrexia was a more noticeable feature than in those where there was no tuberculous infection, and vomiting was much more commonly present.

Save for the rigidity of the neck, the cases more nearly resembled tuberculous meningitis than those infected by the diplococcus intracellularis.

In addition to the cases here reported, there were admitted to the London Hospital during the year 1901 seventeen cases of tuberculous meningitis, as shown by post-mortem examination, the cerebro-spinal fluid of which proved sterile.

Further, there were thirty-five other cases admitted presenting the clinical characteristics of acute cerebro-spinal leptomeningitis, but of which it was not possible to determine the infecting organism; of these, sixteen recovered and were discharged, and nineteen died.

Fourteen of the fatal cases were submitted to post-mortem examination, and in twelve purulent meningitis was found present, which had apparently arisen apart from any local source of infection; in one there was acute hydrocephalus without any sign of tuberculosis, and in one the condition was described as acute hæmorrhagic leptomeningitis.

Several of these cases were doubtless due to infection by the pneumococcus or by pyogenic organisms, but many seemed in all probability to be cases akin to those infected by the diplococcus intracellularis. They are mentioned to show the frequency with which acute leptomeningitis occurred during the year.

TABLE VII.—*Cases of mixed infection.*

No.	Name and date.	Age.	Onset.	Duration and result.	Rigidities.	Kernig's sign.	Movements.	Vomiting.
32	William A., Sept. 17th, 1901	3 years	Vomiting; constipation	26 days; death	No rigidity of neck at first; rigid later	Indefinite	Dissociated movements of eyes; rest- less	None in hospital
33	William W., March 13th, 1901	1½ years	Irritability; retraction of head; convulsions	26 days; death	Rigidity of neck; at times retraction of head	Present sometimes	Convulsive movements of left arm and leg	Just at end
34	Ethel G., April 15th, 1901	3½ years	Headache for months; vomiting 5 days; constipation	10 days; death	Slight rigidity of neck; some rigidity of limbs	Not present at first; definite later	Occasional strabismus; convulsive movements of left arm and leg, and less so right arm	First week
35	Charles F., April 16th, 1901	½ year	Vomiting; looked ill	14 days; death	Retraction of head; opisthotonos marked; limbs rigid later	Not present	Convulsions; dissociated movements of eyes	Frequent
36	John B., April 20th, 1901	3 years	Cough; fever; diarrhoea	23 days; death	Neck rigid; limbs rigid	Present on left side	Nil	At first
37	Lily G., April 2nd, 1901	10 months	Vomiting and diarrhoea; squint later	18 days; death	Neck rigid	Not present	Strabismus	Through- out
38	Ellen H., June 17th, 1901	5 years	"Tired;" headache; vomited once	24 days; death	Neck rigid	Present	Strabismus; dissociated movements of eyes; irregular movements of limbs	Once



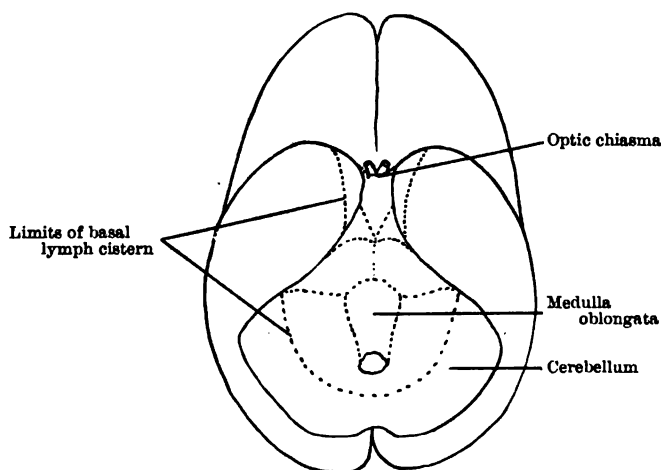
B. tuberculosis and *Diplococcus intracellularis*.

Fundi.	Tempera- ture.	Bacteri- ology.	Meningitis.			Hydrocephalus.	Remarks.
			Vertical.	Basal.	Spinal.		
—	Normal; rose to 100°2'	Diplococcus found in fluid from lumbar puncture	Tubercles along vessels; no lymph	Much lymph at base and under cerebellum	—	Excess of fluid; some lymph in ventricles	Caseous mediastinal gland; no other evidence of tuberculosis.
Normal	100°; rose to 108° before death	Ditto	—	Tubercular meningitis	—	—	Had been attending the hospital 1 year for congenital syphilis; post mortem, miliary tuberculosis of all organs.
Normal	99°—102°8'	Ditto	—	Much lymph; tubercles along vessels	No lymph; excess of fluid (clear)	Slight excess of fluid in ventricles	Miliary tuberculosis of all organs; caseating mediastinal gland.
Normal	99°—100°; 102°4' later	Ditto	—	Lymph at base with tubercles	Tubercles on spinal membranes	Excess of fluid; convolutions flattened	Caseating bronchial glands; miliary tuberculosis of lungs and spleen.
—	Sustained 100°—104°	Ditto	No lymph	Much lymph at base; many tubercles	Excess of fluid; no tubercles; no lymph	Ventricles distended	Caseating bronchial glands; miliary tubercles of lungs and spleen.
—	97°—98°	Ditto	—	Membranes thickened; tubercles along vessels	—	No excess of fluid	Caseating bronchial gland; miliary tubercles in spleen.
Normal	100°—101°	Ditto	Vertical meninges oedematous	Tubercular meningitis	—	Excess of fluid in ventricles	Tuberculous focus in left lung; miliary tuberculosis, lungs, pericardium, and spleen, kidneys, liver.



and the space is merely potential; in other parts—for instance, the fissures of the cortex or the superior surface of the corpus callosum—the bridles are longer, and an actual space is present in which fluid may collect. If the fluid be clear the appearance suggests œdema of the cortex; if purulent it is termed purulent meningitis. At the base of the brain there are certain places where these bridles are much elongated, and thus are produced the arachnoid cisterns of Key and Retzius. In basic meningitis it is found that there is a large collection of fluid in

FIG. 2.

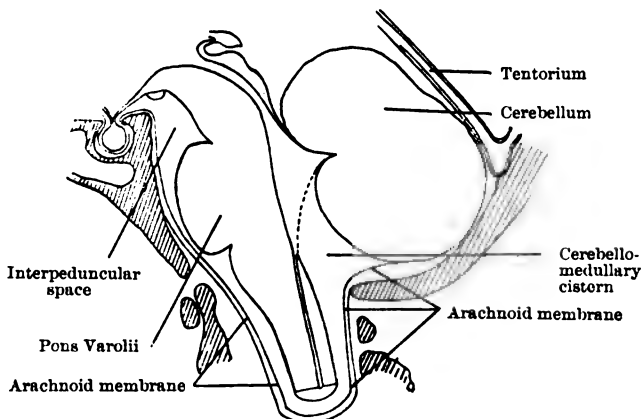


The brain viewed from below to show the limits of the great arachnoid space when distended with lymph.

these cisterns, which are in such free communication that they appear to form one large space bounded by the line of firmer attachment of the arachnoid to brain or cerebellum. Anteriorly the arachnoid seems to be firmly attached along the inner margins of the temporo-sphenoidal lobes, except just at the anterior poles, where the line of firm attachment is somewhat farther out, and from these boundaries to form a kind of bridge over the optic chiasma, the interpeduncular space, and the anterior sur-

face of the pons; below, the space thus formed is continuous with the subarachnoid space of the cord. Laterally the arachnoid is loosely attached round the cerebellar peduncles and over the lobus centralis on the superior surface of the cerebellum, a space being formed which becomes continuous with that on the superior surface of the corpus callosum. Posteriorly the great basal space thus formed passes round the medulla and becomes the cisterna cerebello-medullaris, limited behind when the arachnoid becomes again united to the pia mater on the

FIG. 3.



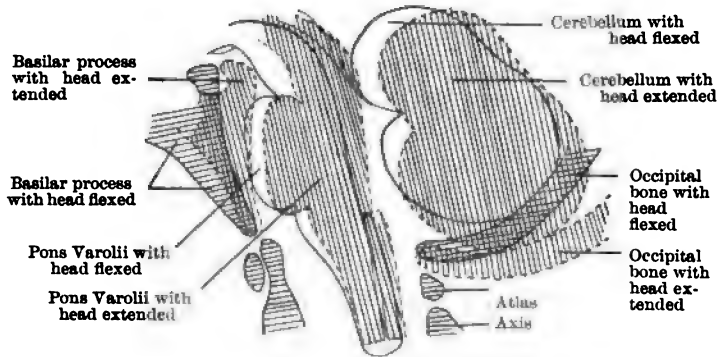
To show the communication of the basal arachnoid cisterns with the spinal subarachnoid space. The arachnoid spaces are shown as if much distended.

under surface of the cerebellum at some distance from the anterior extremity of that organ. The spaces thus marked out can be clearly recognised when filled with purulent material, and, by means of a probe, the situations in which the bridles become shorter can easily be demonstrated, although the greater part of the arachnoid bridge is necessarily destroyed in removing the brain from the skull.

The coloured plate in Allbutt's 'Medicine,' vol. viii, p. 496, shows well the limits of these basal cisterns.

The existence of the cerebello-medullary space is possibly to be explained as an arrangement to permit free antero-posterior movement of the head. In such movement there must necessarily be some sliding of the lower surface of the cerebellum over the medulla: the loose attachment of the arachnoid permits this movement. This sliding of the cerebellum up and down the medulla can easily be demonstrated by removing the bones from one side and base of the skull, and taking out one lateral lobe of the cerebellum. The medulla is thus exposed from the side, and the movement can readily be observed. It can

FIG. 4.



To show the movement of the cerebellum in relation to the medulla in antero-posterior movements of the head. The size of the spaces has been much exaggerated.

be seen almost equally well if, after removal of the cerebrum, a large window be made in one side of the tentorium, and the lateral lobe of the cerebellum be removed through this, so that the medulla is exposed to view. The rigidity of the neck or retraction of the head present, when there is posterior basic meningitis, may be looked upon as protective and preventing mechanical disturbance of the inflamed arachnoid, and comparable in explanation to Kernig's phenomenon. In this connection it is interesting to note that in such cases there is seldom any resistance against rotation of the head round a vertical axis.

The presence of the arachnoid cisterns at the base of the brain permits the collection of lymph in that situation; the subarachnoid space over the vertex is much smaller, and the facility for accumulation of inflammatory products much less. When the convolutions become flattened, in consequence of the rise of intra-ventricular pressure, the space must be still further narrowed. Thus, perhaps, should be explained the predominance of the signs of inflammation at the base when simple meningitis has passed the earliest stage.

This accumulation of inflammatory products in the basal arachnoid cisterns has suggested the use of the term "posterior basic meningitis" to signify the condition. There is no reason, however, to suppose that the inflammation is confined to that region, though the products accumulate there. Many cases which in their clinical characters agree with those described as posterior basic meningitis, show this basal collection of lymph, but also show distinct evidence of inflammation of the vertical meninges, and also of those of the spinal cord. In the circumstances, unless it can be proved that posterior basic meningitis is a distinct and independent disease, it seems best to consider such cases as examples of acute general leptomeningitis in which the inflammatory products have for the greater part accumulated in the basal arachnoid cisterns.

Carr ascribes the strabismus to implication of one or other of the oculo-motor nerves in the inflammatory process. When the extent of the basal inflammation is considered, this would seem to be extremely probable. It is curious, however, how seldom a permanent paralytic squint seems to occur; intermittent strabismus, at times described as a coarse nystagmus or merely as dissociated movements of the eyeballs, is extremely common. Two explanations of this phenomenon offer themselves. Either—owing to depression of the cerebral centres—there is a reversion to a condition existent at an earlier stage of development, an explanation usually offered to explain the

dissociated movements of the eyes of children during sleep, or of most young people during chloroform narcosis; or else it is due to the irritation of cortical or sub-cortical centres by the inflammatory process, and therefore comparable to the irregular movements of the limbs frequently met with in this disease.

In accordance with the view that the squint is not due to implication of the oculo-motor nerve-trunks in the inflammatory process, is the extreme rarity of affection of any other cranial nerve.

Dr. Carr has discussed at considerable length in his paper the views that have been urged with regard to the pathological conditions underlying hydrocephalus.

He takes exception to the view that the increase of the intra-cerebral fluid is due in all cases to the blocking of the foramen of Magendie, and urges that in some cases, as originally described by Merkel, an excess of fluid is found in the spinal meninges.

In the cases here recorded this has been the rule.

It was generally found that there was a slight excess of fluid in the cortical subarachnoid space, producing an cedematous appearance of the meninges, a greater collection at the base in the great arachnoid cistern, the posterior arachnoid cistern, and also in the spinal subarachnoid space.

Excess of fluid in these situations cannot be explained on any mechanical hypothesis, and it seems unnecessary to suppose that the intra-cerebral collection of fluid has a cause different from the extra-cerebral collection. Clinically the effect of withdrawing fluid by lumbar puncture in reducing the tension of a bulging fontanelle, and in the amelioration of symptoms, suggests that there is not in every case an obstruction at the foramen of Magendie.

Finally, if obstruction of the foramen of Magendie were a common cause of hydrocephalus, it would not be unnatural to suppose that in some cases at least dilatation of the central canal of the cord would occur. In none of the cases here reported was this condition found, nor does literature seem to contain records of such cases.

This mechanical view of the pathology of hydrocephalus has been urged against the employment of lumbar puncture as a remedial measure. It seems, however, that this particular argument against the mode of treatment is based upon a fallacy.

A second mechanical view, originally urged by Rilliet and Barthez and subsequently by Bastian, and discussed by Carr, suggests as a cause of the exudation an obstruction of the veins of Galen. In several cases where there was much lymph at the base in the great arachnoid cistern, it was found that this lymph extended round the peduncles of the cerebellum to the anterior extremity of the superior verum. In this situation it is obvious that it might reasonably be expected to lead to obstruction of the venous circulation of the velum interpositum. Such obstruction should lead to distension of the venous radicles; this, as Carr points out, is usual in the veins seen upon the walls of the lateral ventricles. In none of the cases examined, however, was there any evidence of thrombosis, or even distension of the choroid plexus, though this condition might be expected to be consequent upon venous obstruction.

The third view, which supposes the exudate to be inflammatory, seems most in accord with the appearances found upon the post-mortem table. The main objections to this view are based upon the chemical composition of the fluid, which, it is stated, does not suggest an inflammatory origin. Unfortunately it was not possible to investigate fully the chemical composition of the fluid obtained by lumbar puncture, since the intention of the research was to establish the bacteriology of the disease, and the supply was insufficient for the two purposes.

It does not, however, seem that the analyses of cerebro-spinal fluid hitherto made have been classed according to the stage of the disease at which the fluid was withdrawn. The turbidity of the fluid, the presence of lymph in the lateral ventricles, and the microscopical proof of the presence of cellular elements in several cases were at least



suggestive of inflammatory processes. Possibly even the ventricular fluid may have been secreted by the inflamed pia and arachnoid, and passed upward under tension through the foramen of Magendie.

It is conceivable that, as the condition tends to become chronic, the fluid may cease to contain albumen, and it is only at this stage that the fluid is present in sufficient quantity to enable chemical research to be made.

Further investigations in this direction are necessary before the mechanical theories can be fully rejected.

Dr. Carr suggests a combination of causes: a certain degree of inflammation of the ependyma and membranes, with some obstruction in the velum interpositum. The objections that seemed to discount the venous obstruction theory seem still to hold good; in none of the cases examined was there any engorgement or thrombosis of the choroid plexus. Moreover the presence of fluid in the cortical subarachnoid space, in the basal arachnoid cistern, and in the spinal subarachnoid space, cannot be produced by any obstruction at the great transverse fissure of the brain. Probably, therefore, future investigations will show that there is some fallacy in the objection, based upon chemical analyses, against the inflammatory theory. It may yet be shown that there is a form of leptomeningitis with effusion comparable to pleurisy with effusion or the ascites of tuberculous peritonitis.

*Some Observations on the Relationship of the cases here described to Conditions previously described by others.*

In the cases in this paper the constant factor has been the presence of the diplococcus intracellularis of Weichselbaum, or an organism closely resembling it, in the cerebro-spinal fluid.

Starting with this insight into their etiology, it has been possible to group together the cases and to demonstrate that they present from their clinical aspect many

points of resemblance. It has further been shown that the signs and symptoms of the disease vary according to its stage. Thus, some have died apparently from the acuteness of the initial disease; others from secondary complications, of which by far the most important is hydrocephalus; while others have passed safely through both these stages and achieved a recovery either complete or incomplete.

It remains now to discuss the relationship of this disease to conditions previously described. Weichselbaum originally isolated the diplococcus which bears his name from certain cases which were considered to be sporadic instances of epidemic cerebro-spinal meningitis. Recently Still and others have isolated a similar organism from cases which clinically resembled what was originally termed by Gee and Barlow the cervical opisthotonos of infants, and has more recently been included under the title of posterior basic meningitis.

It is still a point waiting for decision whether Weichselbaum's diplococcus, as the Germans and Americans hold, is the specific organism of epidemic cerebro-spinal meningitis, or whether, as the French and Italians believe, that disease is due to a modified form of the pneumococcus, or whether different epidemics may be due to different organisms. These points can only be finally decided by the systematic examination of genuine epidemics.

The cases which Weichselbaum investigated were six in number, and were spread over a period of three years (1885—1887); at the same time there were a few other similar cases in Vienna, but there was nothing of the nature of an epidemic. It is true that in the year 1885 there was an epidemic at Mailberg, in Lower Austria, but it was not suggested that this was a possible source of infection. The clinical account of the cases is brief, but they seem to have resembled the cases described by Sanderson as examples of the epidemic form of the disease.

Netter, in describing a typical case of the epidemic variety, speaks of three stages: firstly, that of invasion, lasting from a few hours to three days; secondly, that of reaction, in which the rash appears and the symptoms are ameliorated; and thirdly, that of purulent meningitis. The average duration of the disease, he says, is about twenty days, and, as a rule, if not fatal, the convalescence is long and tedious.

The signs are those of acute cerebro-spinal leptomeningitis, together with those of a more or less acute septicæmia, indicated by a purpuric eruption, the typhoid state, and the enlargement of the spleen.

The cases now reported show no tendency to division into these stages, and present no septicæmic symptoms.

In the circumstances it is impossible to dogmatise; instances are not far to seek of diseases with a different degree of virulence in the sporadic and in the epidemic forms. It may yet be proved beyond question that the epidemic form is due to the diplococcus intracellularis. For the present it is only certain that there is a group of cases occurring with a sporadic distribution in which an acute leptomeningitis is associated with an organism closely resembling, and probably identical with, that which Weichselbaum, in 1887, isolated from cases which apparently presented somewhat similar clinical characteristics.

The best available description of a series of cases of epidemic meningitis is that given by Sanderson in a report to the Local Government Board in 1865, concerning an epidemic then obtaining in the region of the lower Vistula. The disease as seen by him was characterised by a sudden onset, with shivering, headache, and profuse vomiting, followed in a few hours by confusion of thought and pains in the neck, lumbar region, or abdominal wall; delirium rapidly supervened, and with it retraction of the head; vomiting often ceased with the loss of consciousness. In the fatal cases insensibility ensued, and death generally resulted from respiratory failure, appa-

rently due to a spread of the inflammatory process to the medulla. In other cases there was a prolonged period of nervous depression, marked by frequent relapses to the initial symptoms, which ushered in a tedious convalescence. In very few cases consciousness returned early and recovery was rapid.

The temperature as a rule was raised, being seldom below  $100^{\circ}$ , and generally between  $102^{\circ}$  and  $104^{\circ}$ . It was highest during the period of invasion, and rose again with any exacerbation of symptoms. When the disease attacked children, he said that the diagnosis from tuberculous meningitis might be of extreme difficulty. He did not attach great importance to muscular tenderness, and suggested that it occurs as an interlude to the pain, and as a harbinger of convalescence. Labial herpes was apparently of common occurrence, but he only quotes one case in which there was a petechial eruption, and associated with this at the autopsy there was found to be a considerable enlargement of the spleen.

Post-mortem examination showed a purulent leptomeningitis affecting the meninges of the vertex and base of the brain, the upper surface of the cerebellum, and both surfaces of the cord. In three cases which died before the eleventh day of the disease there was no excess of fluid in the ventricles; in the fourth, which died after eighteen days, it is stated that the ventricles were distended with turbid fluid.

These cases, save that they appear to have been somewhat more severe than those now related, present many points of similarity, both in their clinical history and in their morbid anatomy. With regard to age incidence, he shows that children are affected very much more frequently than adults; thus 318 died who were under fourteen years of age, and only 17 above that age, in the period January 2nd to March 31st, 1865, in the district of Berendt.

Though the disease occurred undoubtedly as an epidemic, Sanderson's conclusion was that "no facts were

met with in the course of the inquiry which afforded ground for believing that epidemic meningitis was capable of being communicated by personal intercourse," a statement that is equally true for that occurring in East London in 1901.

Gee and Barlow, in 1878, described and named the condition known as the cervical opisthotonos of infants, and have since continued the investigation of the disease. From the first they suggested a possible relationship to epidemic cerebro-spinal meningitis, but it was not until Still, in 1898, succeeded in isolating an organism which only differed in minor details from that described by Weichselbaum, that the alleged connection became a pathological probability.

There can be no doubt but that many of the cases here described could very reasonably be diagnosed as "posterior basic meningitis;" the point seems to strengthen the credibility of Gee and Barlow's supposition, and also establishes the fact that this disease, though occurring with greater frequency in young children, may occur at least up to the age of thirty-five. The localisation of the purulent exudate to the base of the brain may possibly be explained by the stage of the disease at which the autopsy was performed. In the later stages of the disease it seems to be the rule that the purulent matter remains longest in the basal arachnoid cistern, where at the height of the disease it has existed in greatest quantity.

That the disease may be the cause of acute hydrocephalus is proved by some of the cases quoted; that it may lead to chronic hydrocephalus with enlargement of the skull is probable. Two cases (Dorothy R—, Case 14, and Henry P—, Appendix II) are here given in support of this view, and Dr. Ainley Walker permits me to state that he has isolated Weichselbaum's diplococcus from a case of chronic hydrocephalus which occurred at Guy's Hospital.

Hanshalter<sup>1</sup> has recently reported a case of chronic

<sup>1</sup> 'Les Cliniques Médicales Iconographiques,' p. 127, March, 1902.

hydrocephalus in a child aged six weeks, which was secondary to pneumococcal meningitis; unfortunately, however, the cultural reactions of the organism are not recorded, so that bacteriological certainty is not obtained with regard to the nature of the organism. It does not, therefore, seem improbable to suppose that many cases of chronic hydrocephalus, first becoming manifest after birth, may be not idiopathic, but secondary to an antecedent meningitis.

Bastian, in the last edition of Quain's 'Dictionary of Medicine,' is not inclined to think that this is a common event; it is a point that can only be settled by following up the subsequent history of cases which have been known to suffer from acute leptomeningitis before synostosis of the cranial vault, and from which a definite organism has been isolated.

*Conclusions.*—Passing these considerations in review, it seems necessary to arrive at the following conclusions:

1. That infection by the diplococcus intracellularis of Weichselbaum has been shown to be associated with a train of symptoms to which have been applied the names epidemic cerebro-spinal meningitis, cervical opisthotonos of infants, and posterior basic meningitis.

2. That these conditions are therefore identical in their etiology, and are probably identical with certain epidemics of cerebro-spinal meningitis which occurred before the introduction of bacteriological methods of diagnosis.

3. That cases of chronic hydrocephalus sometimes are consequent upon this form of acute meningitis.

#### TABLE IX.

A comparison of the clinical characters of—

- (1) Epidemic cerebro-spinal meningitis as described by Netter in 'Twentieth Century Practice of Medicine.'

- (2) Posterior basic meningitis as described by Still in Allchin's 'Medicine' (1901).

- (3) The cases reported in this paper.

	Epidemic cerebro-spinal meningitis (Netter's description).	Posterior basic meningitis (Still).	Cases reported in this paper.
Age	Up to 35 (children especially)	Common in first year, rare after second year	2 months to 35 years.
Evidence of spread by contagion	Nil	Nil	Nil.
Epidemics among persons closely associated	Yes	Nil	Nil.
Onset	Sudden	Sudden	Rapid.
Headache	Present early	Impossible to detect	In older patients.
Vomiting	Present	At onset and often throughout	At onset and commonly in later stages.
Constipation	Common at onset	Not common	Not common.
Rigidity of neck	Common	Constant	In all but one case.
Rigidity of limbs	At times	Common	At times.
Kernig's sign	Common (45 out of 50)	Common	13 out of 22.
Temperature	Pyrexia early; 102°	Irregular pyrexia 2 to 3 weeks	Pyrexia early; normal later.
Pulse	Infrequent at onset; accelerated later	Frequent throughout	Frequent throughout.
Respiration	Often periodic	Periodic towards end	Periodic towards end in some cases.
Emaciation	Rapid	Rapid	Rapid.
Mental disturbance	Profound and early	Impossible to detect	In the older cases.
Champing of jaw	At times	Common	Common.
Convulsions	At times	Sometimes at onset; common later	Sometimes early; common later.
Retraction of lids	No mention	Common after 3rd and 4th week	Common in later stages.
Hydrocephalus	Sometimes a sequel	Common sequel	Common sequel.
Photophobia	Common	—	Not common.
Blindness	Sometimes	One third of cases	Common.
Strabismus	Sometimes; varies in different epidemics	Transitory if present	Dissociated movements of eyes common.

	Epidemic cerebro-spinal meningitis (Netter's description).	Posterior basic meningitis (Still).	Cases reported in this paper.
Optic neuritis	No mention	Uncommon	Uncommon.
Rashes	On 3rd day; (a) herpes labialis; (b) petechiæ; (c) rose rash	Rare	Rare.
Stage of improvement with eruption	Present	Not present	Not present.
Joint pains	Common	4 in 40 cases	No instance.
Definite stages	(1) invasion; (2) reaction; (3) stage of purulent meningitis	—	(1) Stage of meningitis; (2) Stage of hydrocephalus.
Duration	Average about 20 days	Up to 3—4 months	3 days to 6 months.
Sequelæ	Generally none; sometimes neuralgia, paralysis, deafness, amaurosis, hydrocephalus, mental troubles	Hydrocephalus; idiocy or imbecility	Hydrocephalus; imbecility; blindness; deafness; spastic rigidity of limbs, etc.
Diagnosis from	Typhoid, typhus, influenza	Tuberculous meningitis; secondary meningitis; head retraction, due to disease of teeth or ears	Tuberculous meningitis; secondary meningitis; typhoid; influenza; cervical caries, or retropharyngeal abscess; head retraction, due to disease of ears or inflamed glands secondary to impetigo of scalp.

### HISTORICAL SURVEY.

The history of scientific progress in the study of meningeal disease has been so frequently and so well reported, and within so recent a period, that a full and complete account is rendered unnecessary.

Such accounts, however, have, as a rule, treated the subject from one particular aspect alone, and for this reason an attempt has here been made to mass together in one short account a series of references to the chief



discoveries that have marked the progress of this branch of medical science.

Chronological order, so far as was possible, has been maintained, and an attempt has thus been made to show how several diseases, at one time considered distinct, have, with the progress of knowledge, been proved to be related one to the others.

A bibliographical record has been appended giving references to works of which mention has been made, and showing where a more complete account of the literature, which has now become so vast, may be obtained.

In the earliest medical literature no evidence can be found to suggest that inflammation of the coverings of the brain was looked upon as a disease; that the disease then existed may be inferred from descriptions of conditions which, in all probability, represented the secondary effects.

The year 1768 marked the dawn of a new era in the study of cerebral disease. Robert Whytt, of Edinburgh, recorded his memorable observations upon acute hydrocephalus; most, if not all of his cases were due to tuberculous meningitis, but he thought that the determination of the fluid to the ventricles was primary and the cause of the disease. His description of the clinical characteristics of the condition and their division into the three stages form the boundary between chaos and order in the history of intra-cranial inflammatory disease. In conformity with the conception that the effusion was primary and all-important, he employed the title "acute hydrocephalus," a term which continued in general use until 1825, when Senn urged the propriety of substituting the word meningitis.

The work of Whytt was soon followed by that of other investigators. Quin, of Dublin, in 1780 is to be credited with the suggestion that the effusion in the ventricles was secondary, but he went no further than to suggest as a cause a morbid state of the blood in the cerebral vessels.

In the same year Edward Ford suggested, as possible

causes of the dropsy, inflammation of the pia mater, or a tuberculous induration of the brain or cerebellum.

In 1789 Isaac Rand presented a report to the Massachusetts Medical Society on 'Hydrocephalus Internus,' in which he states that "it is probable that the effusion of water into the ventricles of the brain is the effect of inflammation of the meninges." He quotes Whytt, and credits Quin with the recognition of the secondary nature of hydrocephalus, but does not seem to have been familiar with the work of Ford.

Thus at the end of the eighteenth century it seems to have been generally recognised that acute internal hydrocephalus was secondary to some antecedent meningeal or vascular disturbance. At the commencement of the nineteenth century inflammatory conditions of the cerebral meninges came to be recognised as associated with certain symptoms.

Herpin, in 1803, a surgeon with the Army of the Rhine, introduced the term meningitis to express inflammation of the meninges.

The cases that he describes were secondary to fracture of the skull, and consequently unimportant from the point of view of this research. His analysis of symptoms, however, and their contrast with those of what he termed encephalitis, which apparently followed concussion without fracture of the skull, formed a useful basis for those who subsequently investigated the primary form of the disease.

Herpin's seems to have been the first attempt to associate definite symptoms with inflammation of the meninges apart from hydrocephalus. In 1806 there occurred at Geneva an epidemic of a disease with which the physicians of the time were not familiar; it was described by Vieusseux under the title "*fièvre cérébrale maligne non-contagieuse*." This disease occurred in several members of the same household, but apparently was not communicable by personal contact. It affected chiefly children and young adults, nine tenths of the cases being under thirty years of age, and was not particularly dan-

gerous. The onset was sudden, with headache, vomiting, and delirium, and it might prove fatal in twenty-four hours. In the cases that were not fatal the recovery was rapid and complete, the longest duration being fourteen days.

Unfortunately the report of the post-mortem appearances is unsatisfactory, and in the allusions made to the autopsies there is nothing to suggest that purulent inflammation of the meninges was ever found.

It has, however, been usually accepted that this is the first account of what is now known as epidemic cerebro-spinal meningitis. Mathey gives an account of one autopsy which he conducted for Vieusseux, and describes a gelatinous condition of the meninges which may possibly be taken to indicate the presence of meningitis.

In the same year (1806) Danielson and Mann described an outbreak of a similar disease which occurred in Medfield, Massachusetts, giving the symptoms of the disease and the result of five autopsies. In 1809 a committee, consisting of Drs. Jackson, Warren, and Welch, presented a report concerning this epidemic. They concluded that though it was termed "spotted fever," yet "the petechiæ were secondary and not essential to the disease;" it was a fever of which the "greatest stress fell on the membranes, especially on those within the cranium." They suggested that this inflammation was commonly erysipelatous in nature. The Geneva and the Medfield epidemics drew attention to a disease previously unrecognised, and though there can be no certainty that it was the same as that now known to be caused by the *diplococcus intracellularis*, yet the investigations that followed laid the foundation for our subsequent knowledge of the subject.

In 1814, Biëtt, in a Paris thesis on acute idiopathic phrensy, complained that the term was commonly, though wrongfully, applied to inflammation of the arachnoid. Apparently he was the first who recognised idiopathic meningitis as a separate disease, and realised that acute hydrocephalus may follow inflammation of the arachnoid.

In 1815, Golis, in a treatise on acute hydrocephalus, defined dropsy of the head and brain as "a collection of serous, lymphatic, or puriform fluid, or a mixture of these, in the cavities of the cranium or in those of the brain."

This he said might be—

(A) External—that is, either between the scalp and pericranium, or between the pericranium and cranium.

(B) Internal—that is, (a) between cranium and dura mater; (b) between dura mater and pia mater; (c) between pia mater and brain; (d) in the cavities of the brain.

(c) Combined, external and internal.

From the description he gives of the cases it seems clear that he dealt with cases not only of tuberculous meningitis and of idiopathic meningitis, but also with cases of secondary meningitis due to fracture of the skull, and possibly also to middle ear disease. In one case in which death resulted from convulsions during an attack of whooping-cough, the record of the autopsy scarcely seems to justify his diagnosis of acute hydrocephalus, seeing that apparently there was no meningitis and no excess of fluid in the cerebral ventricles.

He distinguished two groups of cases which could be recognised by the mode of onset. In the first group the symptoms developed gradually, and apparently closely corresponded to those of what is now recognised as tuberculous meningitis. The second group resembled in the symptoms and mode of onset the posterior basic meningitis of recent years; the disease, he says, commenced suddenly with headache, vomiting, fever, and retraction of the head; and he remarks that the prognosis in this form is better than in the first group; the duration he gives as between thirteen and twenty-one days, and recognises four stages corresponding to the pathological conditions of convulsions and paralysis. In 1809 he had apparently to deal with an epidemic of acute cerebral meningitis amongst the children of Vienna.

Golis, therefore, though he apparently did not clearly differentiate between primary and secondary meningitis,

was able to recognise in his practice cases which corresponded to these groups, and, by drawing a distinction between external hydrocephalus, which in some cases at least was associated with secondary meningitis, and internal hydrocephalus, made an important advance in the study of meningeal disease. Moreover in the matter of internal hydrocephalus he foreshadowed, from clinical experience, a distinction between tuberculous and other forms of acute meningitis, which bacteriological research has since been able to confirm.

Two years later, Coindet, writing about hydrocephalus, includes as causes many other conditions besides meningitis. He gives an account of a case of acute tuberculosis of the lungs, associated with tuberculous meningitis, in a child aged thirty months, but also describes cases of tumours of the brain and pons Varolii, of meningitis associated with otorrhœa, and of acute scarlatinal nephritis with uræmic convulsions, as instances of acute hydrocephalus.

He points out that the condition tends to occur in epidemics:

“Il y a plus grand nombre d’hydrencéphales que dans aucune autre époque pendant les épidémies de fièvres catarrhales. On voit le principe inflammatoire se porter d’emblée sur le cerveau—d’autre fois en le voit se porter d’emblée sur la poitrine—et la quitter pour se jeter sur le cerveau.” He noticed that an effusion into the ventricles took some time to form: “Il résulte donc de cet examen cadavérique que dans les morts promptes, il y a peu d’eau, ou que même il n’y en a pas du tout, et qu’il y a beaucoup d’engorgement sanguin; que lorsque la maladie a duré trois semaines ou plus, il y a beaucoup d’eau et moins d’engorgement.”

With regard to the cause of the ventricular effusion, he expresses a strong belief that it is due to inflammation of the lining membrane of the ventricles: “L’épanchement dans les ventricules est l’effet et non pas la cause de l’irritation fébrile ou de l’inflammation.” The distension

of the ventricles, he thought, caused symptoms of compression or of apoplexy; if not fatal, the effusion, he supposed, might subside completely, or in some instances give rise to chronic hydrocephalus.

Considering these statements, it seems necessary to suppose that he must have observed cases of acute meningitis not due to the bacillus tuberculosis; moreover his deductions seem closely in accord with those reached in the present research.

In agreement with Coindet's views, Senn, in 1825, suggested the use of the term "meningitis" in reference to "acute hydrocephalus," and so began a new chapter in the history of meningitis.

During the next twenty years research was devoted toward the separation of different varieties of meningitis.

In 1827 Guersant recognised a granular form of meningitis, but was not certain that the granules were really tubercles. Papavoine, in 1830, speaks of tuberculous arachnitis and meningitis, but Gerhard, in 1834, was the first to satisfy his contemporaries, by an exhaustive research, that the granules were identical with tubercles.

Guersant, in 1839, in an article on meningitis in a Dictionary of Medicine, makes a distinction between tuberculous meningitis and the non-tuberculous or simple form; the latter, he says, is not uncommon among the newly born, and he quotes Albert (1830) to show that it may possibly occur with an epidemic distribution; neither his work, however, nor Albert's, was based on any extensive investigation of the post-mortem appearances.

In a text-book of diseases of children, published in 1843 by Rilliet and Barthez, is to be found the first accurate description of simple non-tuberculous meningitis, the account of the morbid anatomy being based upon the examination of six cases. They recognised three anatomical forms of meningitis:

1. Inflammation of the pia mater with tuberculous granulations in the meninges.

2. Inflammation of the pia mater without any tuberculous granulations in the meninges, but with general miliary tuberculosis of other organs.

3. Inflammation of the pia mater without any tuberculous granulations in any organ of the body.

The first two groups represent well-known varieties of tuberculous meningitis; the third group, they said, was characterised by pus upon the convexity of the brain, and also at the base, especially near the large vessels, with a slight amount of turbid fluid in the ventricles. In the one case in which the cord was examined there was purulent spinal meningitis.

They further endeavoured to differentiate between idiopathic meningitis and that form which was secondary to an antecedent pneumonia or typhoid or other disease.

Of the idiopathic variety the symptoms were headache occurring early and a disturbance of the mental processes, often resulting in delirium occurring before the third day; vomiting generally occurred at the onset, and sometimes continued until death. The trunk and limbs were rigid and convulsions were common; strabismus was frequently noted, and the patients were often blind. Constipation was only present in two out of the six cases. The duration ranged between one and a half and nine days.

The diagnosis generally had to be made from tuberculous meningitis, and in a table of the chief distinguishing features it is shown that in simple meningitis the onset is more sudden, the headache more intense, the course is more rapid, and the duration much shorter. The pulse is commonly rapid throughout, and does not conform to Whytt's stages.

They held that meningitis in children was, in the vast majority of cases, associated with the tuberculous diathesis, but that a simple form occurred, especially among the newly born. They believed that sometimes epidemics of simple meningitis arose, agreeing in this point with Guersant, and also quoting Albert.

There can be but little doubt that they foreshadowed the work of many subsequent investigators, and arrived at conclusions that have been, after many years, amply confirmed.

Concerning the mechanism by which the effusion in acute hydrocephalus is determined, they put forward a mechanical theory. After discussing the various views that had been previously urged, they point out that if the effusion is due to venous obstruction this must be situated in the course of the veins of Galen, or of the straight sinus, since these are the only veins that drain the ventricles. They say that in some instances they found such obstruction, but that in others no lesion was found in or near these channels, and in consequence suggest that possibly compression occurs as a result of pressure transmitted from below through the cerebellar substance.<sup>1</sup>

In 1844, Gillkrest, an English army surgeon, published an account of an epidemic of meningitis which occurred in that year at Gibraltar. This epidemic was not confined to children, but chiefly affected those between two and eighteen years of age. The onset was sudden, with headache, strabismus, deafness, blindness, etc., and either death occurred on the fifth or sixth day, or marasmus supervened, which might end in death at a later period of the disease, or in recovery after a protracted convalescence. He drew attention to the head retraction and opisthotonos, which was common, and which does not seem to have been noticed by previous authors. He was unable to obtain leave for post-mortem examination upon any children; in the adults he found lymph upon the vertex of the brain, and "the most unequivocal marks of inflammation at the base of the brain." Sometimes he found lymph down the spinal cord; occasionally there was a great excess of fluid in the ventricles. He was familiar with the granular meningitis of Guersant, but

<sup>1</sup> Bastian, in 1867, again put forward the view that the effusion may be the result of thrombosis of the veins of Galen.



did not meet with that condition in any of his cases. Gillkrest undoubtedly had to deal with cases which conformed to the group that Rilliet and Barthez had described under the name of simple meningitis, and his work was the first which gave the evidence of morbid anatomy in support of their view that the disease might occur in an epidemic form. Moreover, seeing that his practice was not confined to children, he was able to show that it might occur in later life.

The next important contribution to the study of meningeal disease was made by Hilton in his lectures on 'Rest and Pain,' where he suggested his famous mechanical theory for the production of internal hydrocephalus. He supposed that owing to a congenital condition, or to previous inflammation in that region, the foramen of Magendie became blocked, so that the draining of the cerebro-spinal fluid from the ventricles was prevented. The probability of the explanation has been discussed elsewhere; it was so specious, and emanated from so high an authority, that it has loomed largely, perhaps too largely, in the writings of subsequent investigators.

Later, in 1865, Burdon Sanderson presented a report to the Privy Council concerning an epidemic of cerebro-spinal meningitis then prevalent in the region of the lower Vistula. This report, containing an accurate account both of the clinical characters and of the morbid anatomy of the disease, with an investigation of its epidemiology, forms the first trustworthy standard to which reference can be made in determining the identity of other outbreaks to which a similar name has been applied. He established an important point in that he showed that "no facts were met with in the course of the inquiry which afforded ground for believing that epidemic meningitis was capable of being communicated by personal intercourse." In times when bacteriology could not be invoked to determine the etiology of a disease, evidence of transmission by contagion was an important point for investigation; meningitis, it is now admitted, may be due to infection by several different

organisms, and it is quite probable that the mode of infection may be different with different varieties. Sanderson showed that one variety of meningitis at least could be epidemic, though not spread easily by contagion; granting similarity in clinical characters and in morbid appearances, evidence concerning the mode of spread must weigh heavily in forming a judgment concerning the nature of two independent outbreaks.

Webber, writing in 1866, in reviewing all the past literature concerning epidemic meningitis, concludes that "it is only epidemic typhus, wherein, from some cause, the cerebro-spinal system is the principal seat of the attack."

The clinical characters of the cases recorded by Sanderson do not suggest any relation to typhus, and the absence of evidence of spread by contagion seems to render such a relationship highly improbable.

Murchison admitted that meningitis might be a complication of typhus; it seems a natural deduction that some of Webber's cases at least may have been diagnosed erroneously, and that they did not belong to the same group as Sanderson's cases, but were due to some other infection, possibly that of typhus.

Since this time, however, epidemic cerebro-spinal meningitis has been recognised as a distinct and independent disease characterised by a definite group of symptoms. It was from cases belonging to this type that Weichselbaum, in 1887, isolated the organism which bears his name, and which is supposed to be the infecting agent.

In 1878 Gee and Barlow published a paper concerning the cervical opisthotonos of infants, but although they suggested its possible relationship with epidemic meningitis, they were unable to find evidence of transmission by contagion, and did not consider that the disease occurred with sufficient frequency to deserve the title of epidemic. In all, they investigated twenty-five cases, the oldest of whom was aged nineteen months; the onset, they said, might be sudden or gradual, and the retraction of the head, which suggested the name, was associated with

rigidity of the limbs and sometimes with epileptiform convulsions. Sometimes enlargement of the head occurred. At the autopsies basic meningitis was found without any evidence of tuberculous infection; in two cases spinal meningitis was present, in one there was internal hydrocephalus, and in five a small effusion into the ventricles.

These cases seem closely allied to the condition described by Rilliet and Barthez as simple meningitis; retraction of the head, however, had not been previously noticed as a prominent feature of the disease, except by Gillkrest in the epidemic at Gibraltar. These cases have more recently been included under the heading of "posterior basic meningitis."

With the development of methods of bacteriological research a new epoch in the study of meningeal disease was inaugurated.

In 1882, Koch, by his discovery of the tubercle bacillus, rendered it possible to be certain concerning the etiology of tubercular meningitis. During the next few years numerous authors described organisms which they considered to be the causal agents of epidemic meningitis, but it was not until 1887 that an accurate description with cultural reactions was given by Weichselbaum of an organism isolated from the cerebro-spinal fluid of certain cases of cerebro-spinal meningitis. Weichselbaum dealt with eight cases, and they occurred during the years 1885, 1886, and 1887.

From two cases he isolated the pneumococcus; from the remaining six he obtained an organism to which he applied the name *diplococcus intracellularis meningitidis*, or, briefly, *meningococcus*.

The cases with which Weichselbaum dealt were sporadic, and from the brief clinical report they seem to have conformed to the type investigated by Sanderson on the lower Vistula, and not to the type described in some epidemics where the hæmorrhagic tendency and enlargement of the spleen are so suggestive of a septicæmic condition.

About this time (*i. e.* 1886 and 1887) Netter and Foa

and Ufferduzzi isolated the pneumococcus from cases diagnosed as epidemic cerebro-spinal meningitis.

Both the pneumococcus and the meningococcus have been frequently isolated by other observers since that time; it is unquestionable that both organisms may give rise to cerebro-spinal meningitis, and it is generally admitted now that they are distinct. It has not, however, been finally settled whether the epidemic form of the disease is always due to infection by the same organism. Differences in the clinical manifestations suggest that all epidemics do not claim the same infective agent.

In 1891 Wynter showed that in cases of tuberculous meningitis the ventricles could be drained by opening the spinal theca in the lumbar region, thus casting doubt upon the truth of Hilton's mechanical theory of the production of hydrocephalus. In the same year Quinke described the process of lumbar puncture, which has since proved to be of such great value in determining the nature of the bacterial infection.

In 1893 Merton demonstrated that hydrocephalus might exist without closure of the foramen of Magendie, and thus supported Wynter's objection to Hilton's theory.

In 1897 Dr. Walter Carr published a long and accurate description of the posterior basic meningitis of infants, entering fully into the clinical aspect and morbid appearances, and discussing at length the pathological conditions which gave rise to the various symptoms. This is the first important paper that deals with this subject since the publication of Gee and Barlow's cases; unfortunately it lacks bacteriological confirmation. This was supplied in the following year by Barlow, Lees, and Still in their article in Allbutt's 'System of Medicine,' in which, in addition to an accurate clinical account of the condition, is recorded Still's observation that an organism closely resembling, if not identical with Weichselbaum's meningococcus, was the infecting agent.

Thus bacteriological evidence was supplied showing the probability of the relationship of posterior basic meningitis

to epidemic meningitis, a relationship which on clinical grounds had been surmised by previous authors.

In the same year (1898) appeared the report of Councilman, Mallory, and Wright, concerning a number of cases of cerebro-spinal meningitis from many of which they had isolated an organism which in its morphological and cultural reactions they considered to be identical with Weichselbaum's diplococcus. The frequency of occurrence of the disease so far transcended the normal that the adjective "epidemic" seemed justifiable. There was no evidence of spread by contagion, and the clinical accounts of the cases show that they were similar to those described by Sanderson, and to those from which Weichselbaum isolated his meningococcus. In this paper 111 cases were reported, and in thirty-nine of these the infecting organism was isolated and cultivated; in most of the other cases the bacteriological diagnosis was based upon the finding of intra-cellular diplococci resembling the meningococcus by microscopic examination of the cerebro-spinal fluid, the nasal secretion, or aural discharge. In the remainder the diagnosis was based upon the clinical characteristics. Since this time, in America and Germany at least, the specificity of the organism has been deemed established.

In 1899, Netter, whose familiarity with the disease is well known, and whose researches have been spread over so long a period, published a long and important article in the 'Twentieth Century Practice of Medicine,' dealing with the disease from all aspects—clinical, pathological, epidemiological, and historical. He claims that in certain epidemics, at least, the pneumococcus is the infecting agent, and seems not quite convinced that the meningococcus is not an attenuated form of the pneumococcus. He does not attempt to draw any clinical distinction between cases infected by the pneumococcus and those due to the meningococcus.

Netter's weighty opinion has carried with him the French and Italian schools of thought, it being generally

held in those countries that the pneumococcus is the organism of epidemic cerebro-spinal meningitis.

It seems scarcely possible to settle this point until an epidemic of a disease whose symptoms resemble those of malignant fever occurs and is submitted to systematic bacteriological investigation.

In 1899 Osler delivered the Cavendish Lecture on cerebro-spinal meningitis; he believed that the meningococcus was the specific organism of epidemic meningitis, but was fully aware of the possibility of infection by the pneumococcus.

In 1901 Thursfield published some cases which confirmed Still's observation that posterior basic meningitis could be produced by an organism resembling the meningococcus; and a few months later Hunter and Nuthall recorded the bacteriology of the cases related in this paper.

In 1902 Hanshalter published a case of chronic hydrocephalus which, from microscopical examination, he concluded was the result of infection of the meninges by the pneumococcus.

In the present paper, basing the diagnosis upon the bacteriological examinations made by Hunter and recorded by him in the 'Lancet,' an attempt has been made to analyse the conditions produced when this organism attacks the meninges. For this purpose, as has been explained, the cases selected are those only in which a complete bacteriological examination was possible.

Infection of the meninges by the diplococcus has thus been shown to produce symptoms suggesting identity with the disease described by Gillkrest, Sanderson, Weichselbaum, Councilman, and many others as epidemic cerebro-spinal fever, and also with the disease hitherto supposed to be limited to childhood, and described by Guersant, Rilliet and Barthez, Gee and Barlow, Carr, Still, Barlow and Lees, and Thursfield, as simple meningitis, cervical opisthotonos, or posterior basic meningitis. Finally, it has been shown that infection by this organism may be one of the causes of chronic hydrocephalus.

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#### APPENDIX I.

CASE 1.—Kate A—, aged 8 months, admitted April 4th, 1901, died April 5th, 1901. The child was admitted under the care of Dr. Gilbert Smith on April 4th, having been ill one day. The child was breast-fed, and previously had been healthy; the illness started with a fit.

There were signs of broncho-pneumonia in the chest, and there were purpuric spots over the body. There was no retraction of the head, and Kernig's sign was not present.

The next day it was noted that the left pupil was larger than the right, and that both reacted to light. There was some squinting with continuous rhythmical up-and-down movement of the eyeballs. There was some rigidity of the neck, but no retraction of the head. Kernig's sign was not present.

She died quite suddenly.

The temperature on admission was  $100.9^{\circ}$ , and rose to  $105.4^{\circ}$  just before death.

At the post-mortem examination there was no evidence of tuberculosis; scattered patches of lymph were found at the base, on the vertex, and down the cord. There was an

excess of fluid in the lateral ventricles, which Dr. Hunter reported to contain the diplococcus meningitidis in pure culture.

CASE 2.—Sarah H—, aged 7, admitted February 19th, 1901, died February 22nd, 1901. The patient had been quite well until six days before admission under Dr. Schorstein, when she began to complain of headache and nausea, and vomited once. She had been getting thinner during the week, and for the last twenty-four hours she had been very restless, screaming a great deal, and had had incontinence of urine.

The child lay curled up in bed with the limbs flexed and the head retracted; she was very irritable, and when uncovered asked petulantly for the bedclothes.

No signs of disease were found in the thorax or abdomen. There was no otorrhœa, and no sign of injury to the head. There was left internal strabismus. The fundi, except for a little fulness of the veins, appeared normal. Kernig's sign was well marked. Lumbar puncture was performed and several drams of clear fluid withdrawn, and from it the diplococcus intracellularis was isolated. On February 21st some twitching movements of the arms and face followed an ophthalmoscopic examination; later these movements recurred, chiefly in the face and right arm.

The temperature on admission was  $103^{\circ}$ , and rising, it continued between  $104^{\circ}$  and  $103^{\circ}$  until death.

There was no vomiting.

At the post-mortem examination no evidence of tuberculosis was found in any of the organs. On the vertex of the brain the cortical vessels were markedly congested, and there were scattered patches of dry purulent lymph with a considerable excess of clear fluid in the interpeduncular space. The ventricles were filled with clear, slightly blood-stained fluid; the ependyma had not lost its polish. From top to bottom of the cord there were scattered patches of purulent lymph. There were no coarse patho-

logical changes in the substance of the brain or cerebellum.

CASE 3.—Harry G—, aged 7, admitted April 29th, died May 5th, 1901. Five days before admission under Dr. Stephen Mackenzie it was noticed that the boy had incontinence of urine, but, seeming apparently well in other respects, he was allowed to go to school as usual. Three days before admission he went to a swimming bath, where he had a fall, which, however, did not seem serious; in the evening he developed a cough. Two days later his mother was bringing him to the hospital on account of the cough, when he had a fit, and he was still in convulsions when he was admitted.

The fits were repeated at short intervals, being epileptiform in character; there was no return to consciousness between the fits. Lumbar puncture was performed at once, and the symptoms seemed to be temporarily relieved; the fluid was under considerable pressure and spurted out of the tube. The meningococcus was found to be present. In the evening there was found marked retraction of the head; there was restlessness but no twitching. The kneejerks were not obtained. The next day he seemed torpid and the retraction of the head continued, and Kernig's sign was obtained. There was swelling of the optic disc. The stupor continuing, Mr. Openshaw was asked to see the case with a view to surgical interference.

The skull was trephined over the vertex, and continuous irrigation was established from the subarachnoid space to a cannula inserted into the spinal theca in the lumbar region. The patient, however, died eighteen hours after the operation.

Temperature on admission was  $100\cdot4^{\circ}$ , rising in the evening to  $103^{\circ}$ , and then falling gradually to  $96\cdot5^{\circ}$  on April 3rd, when it rose again to  $103^{\circ}$ . Vomiting was frequent throughout.

At the post-mortem examination there was no evidence of tuberculosis of any organs; the meninges were con-

gested, and lymph was found in the usual positions in cerebro-spinal meningitis.

CASE 4.—Joseph B—, aged 4 months, admitted April 18th, 1901, died April 19th, 1901. The child, who had been hand-fed for the past two months, had been wasting for that time; three days before admission under Dr. Gilbert Smith convulsions had commenced, and had been frequently repeated. His mother complained that he screamed almost continually.

On admission there was marked retraction of the head, and Kernig's sign was present. The pupils were equal and reacted to light, and there was no strabismus. The knee-jerks were not obtained.

The pulse-rate was 164 and the respiration rate 64; The temperature was  $102.4^{\circ}$ , rising to  $104.6^{\circ}$  just before death, twelve hours after admission. There was no vomiting either before or after admission.

Lumbar puncture was performed, and the diplococcus intracellularis found in the turbid fluid withdrawn.

Seven days before admission the child had been brought to the surgical out-patient department for a small hernia; the notes state that he appeared marasmic, but apparently there was then no sign of meningitis.

At the post-mortem examination there was no evidence of tuberculosis in any of the organs. There was a large amount of purulent lymph at the base of the brain, and scattered patches of lymph on the vertex and down the cord, especially in the region of the lumbar enlargement.

CASE 5.—Deborah C—, aged 2, admitted April 20th, 1901, died April 22nd, 1901. On admission under the care of Dr. Gilbert Smith the child had been ill for three days with a cough; there had been no vomiting and no fits. The temperature was  $104.6^{\circ}$ , the pulse 100, and the respiration rate 40. There were signs of pneumonic consolidation at the base of the left lung. On the following day continuous rhythmic movements of the right arm were

noticed, with twitching of the face, the mouth being drawn to the right. There was deviation of both eyes to the right, but some strabismus was present. The pupils were equal. The neck was rigid, but the head was not retracted. Kernig's sign was not present, and the knee-jerks were not obtained. The movements ceased at times, and then the right arm appeared to be more flaccid than the left.

The temperature fell in the morning after admission to 98°, but rose again to 106° just before death at four a.m. on the morning of the 22nd. At the post-mortem examination there was no evidence of tuberculosis in any of the viscera. There was some broncho-pneumonia in the lungs. The brain was much congested, and there was turbid purulent fluid at the base, with purulent lymph spreading on to the convexity. There was no excess of fluid in the ventricles.

CASE 6.—Alfred C—, aged 32, drayman, admitted May 26th, 1901, died June 1st. This man, who was an alcoholic subject, said that he had had inflammation of the lungs six years ago, and pleurisy on the right side for a few days three months before the onset of the present illness. On the morning of May 25th he noticed a pain in the right side of his chest; there was no chill at the onset and no cough.

On admission under the care of Dr. Hadley the liver was found to be enlarged, and pleuritic friction could be heard in the right axilla. There were no symptoms or signs suggestive of meningeal implication.

On May 28th it was noted that the patient was noisy and delirious at night; the signs of pleurisy persisted.

On the 30th the signs of pulmonary trouble had disappeared and the patient seemed better, though he wandered a good deal in his talk.

On the following day (31st) the neck was noted to be very rigid, but there was no retraction of the head; the knee-jerks were not obtained, and Kernig's sign was present. He became semi-comatose, breathing stertorously

and sweating profusely. There was incontinence of urine. In the evening he died.

The temperature was  $100\cdot8^{\circ}$  on the evening of admission, and fell to  $98\cdot4^{\circ}$  on May 28th, but after this it rose steadily and reached  $104^{\circ}$  just before death.

At the post-mortem examination adhesions were found at the apices of both lungs, and recent pleurisy at the right base, but no evidence of tuberculosis or of consolidation of the lungs. The membranes of the brain appeared milky, especially along the course of the vessels. There was an excess of fluid in the ventricles. No pus, or even definite lymph was found.

CASE 7.—Alfred L—, aged 19, gasworker, admitted April 7th, 1901, died April 19th, 1901. This man had been at work until the day before admission. On returning home in the evening he had complained of headache and giddiness. He was admitted under Dr. F. J. Smith in a semi-conscious condition, and was very restless, resisting examination. There were no physical signs to suggest the nature of the disease. On the following morning he seemed exceedingly irritable and restless, refusing his food and resenting examination. The eye movements were good in all directions, and the pupils were equal and reacted to light. The knee-jerks were normal. There was some incontinence of urine. There were no signs of thoracic or abdominal disease.

On April 11th he seemed more conscious, recognising his father and speaking rationally. The knee-jerk was readily obtained on the right side, but only just obtained on the left side. The pupils were equal and reacted to light.

On April 12th the right pupil was slightly larger than the left, and both reacted to light; there was some oscillation of the pupils, which was not respiratory. There was slight right external strabismus; there was no retraction of the lids. The neck was markedly rigid, and the arms resisted passive movement to some extent. Kernig's sign

was present. The knee-jerks were both present and equal; on eliciting the plantar reflex, the toes of the left foot moved up, those of the right foot moved down. There was incontinence of urine. Nasal feeding was necessary. Lumbar puncture was performed.

On April 13th he seemed more sensible, and asked for food; in other respects there was not much change.

On April 17th it was noted that he had had diarrhœa with incontinence of urine and fæces for three days. The improvement which had occurred after the lumbar puncture had passed off, and he had relapsed into a semi-conscious condition with retraction of the head.

The pupils were equal and reacted to light; there was no strabismus. Kernig's sign was present. He complained of occipital pain. The temperature ranged between  $98.4^{\circ}$  and  $101.4^{\circ}$ , being generally about  $100^{\circ}$ ; just before death it fell to  $97^{\circ}$ . Diarrhœa was troublesome during the last five days, but he only vomited once while he was in the hospital. The pulse, at first about 80 to 100, rose to 130 per minute towards the end.

At the post-mortem examination no evidence of tuberculosis was found in any of the viscera; all the organs except the brain and cord appeared healthy. The meninges and grey matter were congested; there was a little lymph upon the superior verm of the cerebellum. The posterior surface of the cord was covered with lymph in its entire extent.

CASE 8.—Henry R—, aged 35, admitted March 27th, 1901, died April 13th, 1901. Early in November, 1900, began to have aches and pains all over, chiefly in the head, and was feverish; one week later he had violent pain in the head and neck, and some vomiting, chiefly after food. He was treated at home for a fortnight without improvement, and was then sent to the Brook Fever Hospital with the diagnosis of enteric fever. The medical officer of this hospital has kindly provided the following note:

The patient was admitted on December 11th, 1900, with



a history of a severe headache of three weeks' duration. On admission the patient was delirious, and there was pyrexia which persisted for two weeks; later the temperature became normal, with an occasional rise. For the first ten days there was retention of urine; there was marked tendency to constipation. After the first fortnight there was vomiting every two, three, or four days, often without any apparent relation to food.

Widal's test was negative on December 12th, 13th, and 21st. The knee-jerks were present throughout, the pupils were equal and reacted to light, and with accommodation; the fundi were clear.

There was no nystagmus or deviation of the eyes to the side. He was drowsy, helpless, and slept much. He was sent home at the beginning of March, as there was no improvement, and the diagnosis of enteric could not be sustained. His wife thinks that he was worse on discharge than on admission to the fever hospital. He remained at home for three weeks. Seeing that he was getting more helpless, while the headache and vomiting continued, he was brought to the London Hospital on March 27th, and admitted under the care of Dr. Hadley.

On admission he complained of frontal and occipital headache, which was increased on tapping the skull with the finger; he lay still in bed taking no notice of his surroundings, and moaning from time to time. He understood questions, but his answers were unreliable, and showed that he was only anxious to be rid of them.

There was considerable general wasting. No facial, ocular, or other palsies were detected. There was some nystagmus on extreme movements of the eyeballs. The knee-jerks were much increased, especially on the right side; on this side alone ankle-clonus was obtained.

The plantar reflexes were brisk, the toes moving downwards. With the hips flexed to a right angle, the knees could be extended to about  $145^{\circ}$ . The fundi were normal. There was some hyperæsthesia over the neck and back of the head. There was no photophobia.

There was no evidence of intra-thoracic or abdominal disease. The urine was normal.

The temperature on admission was  $100^{\circ}$ , and continued to be irregular, ranging from  $97^{\circ}$  to  $101^{\circ}$  until his death. There was occasional vomiting throughout; sometimes there was incontinence and sometimes retention of urine; constipation was marked. The irritability continued, and the headache showed occasional signs of intermission.

On April 11th the patient had a right-sided fit, and later in the day had three more. After the last fit he remained stertorous, with divergent strabismus, contracted pupils (reacting to light), and rigidity of the arms and right leg. On April 12th lumbar puncture was performed, three ounces of fluid being drawn off in which the diplococcus meningitidis intracellularis was found to be present. On April 13th he had another fit and died shortly after. The total duration of the illness was over five months.

The post-mortem examination revealed no gross pathological changes except in the cranial cavity. On removing the dura mater there was found to be a small hæmorrhage into the pia mater at the upper part of the right Rolandic area. The convolutions were much flattened. There was a large quantity of clear fluid at the base of the brain, with thickening of the arachnoid. There were adhesions between the prefrontal lobes and in both Sylvian fissures. There was a large quantity of clear fluid in the ventricles, and at the lowest part of each posterior cornu there was a tiny mass of green lymph.

CASE 9.—Fanny S—, aged  $2\frac{1}{2}$ , admitted February 14th, 1901, died March 27th, 1901. The child was admitted under Dr. Sansom with the history that she had been ill for two months, the chief symptoms being vomiting and wasting. She was found to be greatly emaciated and very irritable, crying out when she was touched or the bed-clothes moved. If undisturbed she seemed to take notice of nothing. The eyes were depressed, and there was retraction of the upper lids showing the sclerotics above

the corneæ. The abdomen was retracted; grinding the teeth was frequent. There was no marked retraction of the head, no rigidity or paralysis of the limbs, and no squint. No signs of disease were found in the heart or lungs; the fundi appeared normal.

For the first three weeks in hospital the temperature remained mainly subnormal, with occasional rises to  $99.2^{\circ}$  or  $99.4^{\circ}$ . Vomiting was frequent. The wasting continued.

During the last three weeks the stupor deepened, and the irritability was lost, the child taking no notice when touched. The vomiting ceased, but the emaciation progressed. Some rigidity of the ankle-joints developed, and also some dissociated movements of the eyeballs. There were some slight general convulsions towards the end. The temperature continued subnormal, and at the last was only  $96^{\circ}$ . Death seemed to be due to inanition. The day before she died she only weighed 1 st. 3 lbs.

On February 26th lumbar puncture was performed, and the diplococcus intracellularis was found in the fluid thus obtained.

At the post-mortem examination there was no evidence of tuberculosis or other disease in any of the viscera. The cerebral convolutions were flattened, and there was a great excess of fluid at the base of the brain, in the ventricles, and in the spinal canal. The cortex was congested and the convolutions were matted together, especially along the Sylvian fissures. No lymph was seen upon the brain, but there was some yellowish lymph all down the spinal cord, especially in the region of the lumbar enlargement.

CASE 10.—May P—, aged 8 months, admitted April 13th, 1901, died May 18th, 1901. The illness began ten days before admission under Dr. Percy Kidd with "inward fits," since when the head had been retracted and the child had screamed a great deal. She had been fed on Nestlé's milk. The fontanelle appeared normal, the neck was rigid, but there was no definite retraction of the

head. With the hips flexed the knees could not be extended beyond about  $135^{\circ}$ . The pupils were equal and reacted to light; there was no retraction of the lids, and no squint. The fundi appeared normal. The temperature was irregular throughout, ranging from  $99^{\circ}$  to  $101.8^{\circ}$  for the first ten days, then for a fortnight between  $97^{\circ}$  and  $99.8^{\circ}$ , the last ten days being marked by some irregular rises. Vomiting commenced during the second week, and continued to be frequent until the end. The bowels acted freely, but there was no diarrhoea. After a fortnight it was noted that there was occasional retraction of the upper lids, so that the sclerotics were visible above the cornea, and there were also some dissociated movements of the eyeballs, producing an occasional squint. Kernig's sign was present; there were movements as of mastication, and quasipurposive movements of the arms. Examined a day or two before death, the fundi still appeared normal. Lumbar puncture was performed on April 2nd, and a considerable quantity of fluid removed, in which the diplococcus meningitidis was found. The symptoms seemed to be relieved for a time by the puncture; the operation was repeated on May 13th, but no fluid was withdrawn. Ultimately the child died of exhaustion.

At the post-mortem examination it was found that the convolutions were much flattened and the ventricles enormously distended with fluid, which was straw-coloured and contained a few flakes of lymph. The choroid plexuses were firm and infiltrated. There was a large quantity of fluid within the spinal dura mater. There was no evidence of tuberculosis.

CASE 11.—Herbert C—, aged 5 years, admitted July 19th, 1901, died September 5th, 1901. This boy had been subject to attacks of headache all his life. Six weeks before admission to the hospital under Dr. Stephen Mackenzie he had suffered from measles. Three weeks later he had complained of pain in his neck, and five days before he was admitted his neck had become stiff. There

was no history of tuberculosis in the family. On admission there was some rigidity of the neck, but no retraction of the head; the cervical glands were a little enlarged, but there was no evidence of any throat trouble. The limbs were not rigid, Kernig's sign was not present, there was no retraction of the upper lids, and no strabismus. The temperature for the first four days was raised ( $99^{\circ}$  to  $101^{\circ}$ ), and the child was drowsy. There was no vomiting. On July 30th the child was allowed to go to a convalescent home. On August 25th diarrhoea and vomiting commenced, and he was sent back to the hospital. He then complained of pain in the head, and there was some rigidity of the neck; he was drowsy, and there was incontinence of urine. Kernig's sign was obtained, and the retinal vessels appeared full, while the margins of the disc were blurred. There was no evidence of heart or lung disease. On September 2nd the child appeared to be much worse; he seemed to be both blind and deaf so far as could be gathered from endeavouring to get him to take notice of light or sound. The pupils were dilated equally, and did not react to light; the retinal vessels were full, but not tortuous; the margins of the discs were blurred, but no definite swelling could be determined; no hæmorrhages were seen. Kernig's sign was present, and there was some rigidity of both arms and legs, with rigidity of the neck.

Lumbar puncture was performed on September 3rd, and Dr. Hunter reported the presence of the diplococcus intracellularis in pure culture.

The temperature was normal on admission, and gradually rose to about  $100^{\circ}$  to  $101^{\circ}$  just before death on September 5th.

There was no post-mortem examination.

CASE 12.—Winifred H—, aged 3, admitted July 20th, 1901, died August 9th, 1901. The illness commenced with measles one month before admission; a fortnight later, July 8th, she began to complain of pain in the head and legs, with occasional vomiting. Throughout this fortnight

the head was retracted, and the temperature ranged between  $100^{\circ}$  and  $102^{\circ}$ . There was no history of tuberculosis in the family.

On admission under Dr. Sansom there was marked rigidity of the neck, with retraction of the head; there was no strabismus, and no retraction of the upper lids. The child was very fretful and resented interference; the legs were kept flexed, and attempts to straighten them caused screaming, though the straightening could be accomplished. She complained a good deal of headache; she took her food well and did not appear very wasted. Though apparently not blind, she failed to recognise her mother. There was no evidence of heart or lung disease. The child continued in much the same condition until August 7th (nineteen days), when she developed cancrum oris, from which she died on August 9th. During this time the temperature ranged between  $99^{\circ}$  and  $102.4^{\circ}$ , and the weight gradually fell from 1 st. 10 lbs. 3 oz. to 1 st. 8 lbs. 11 oz. There was no vomiting in the hospital. Lumbar puncture was performed on July 31st, and Dr. Hunter reported the presence of Weichselbaum's diplococcus. Post-mortem examination was not allowed.

CASE 13.—William H—, aged  $1\frac{1}{2}$ , admitted April 24th, discharged June 28th, 1901. The child was admitted on April 24th, under the care of Dr. Sansom, with well-marked signs of rickets and a temperature of  $103^{\circ}$ .

There were no signs of thoracic disease; the liver and spleen were enlarged. He was very irritable on examination; the epiphyses of the long bones were enlarged, and there was a well-marked rickety rosary. The fontanelle was patent, but did not bulge; Kernig's sign was present. On April 28th lumbar puncture was performed, and one and a half test-tubes of fluid withdrawn, which was found to contain the diplococcus meningitidis. On May 1st slight retraction of the head was noticed. On May 8th the child had an attack of convulsions lasting about twenty minutes, in which he became cyanosed, and there was

marked retraction of the head. These attacks were repeated three or four times a day for a week.

In the intervals there were restless movements of the head, eyes, and frontal muscles, but no strabismus was noticed. Kernig's sign was not present; there was no rigidity of the arms, legs, or neck, and no retraction of the upper lids, though at intervals the eyes became "staring." The temperature was irregular, ranging between normal and  $104^{\circ}$  for eight weeks, and then became normal. Vomiting occurred at intervals, being most marked when the temperature was high.

An epidemic of measles breaking out in the ward, and the child seeming much better, he was discharged on June 28th.

On July 16th he was again admitted to the hospital, having been ill for a week with cough and shortness of breath; there were signs of general broncho-pneumonia and evidence of measles. There was some retraction of the head.

The temperature was  $102^{\circ}$ . He died on July 20th from exhaustion. There was no post-mortem examination.

CASE 14.—Dorothy R—, aged 8 weeks, admitted June 1st, discharged June 10th, 1901. The child was brought to Dr. Hutchison's out-patients' on May 1st, suffering from hydrocephalus. Her mother stated that the head seemed natural at birth, but that it had been increasing in size during the last week. The child had been fed at the breast, and both mother and father were healthy. Her mother had lost one child from bronchitis and convulsions, and had three other children living, who, however, were subject to bronchitis.

The girth of the head was then 17 inches; on May 25th, when next seen, there had been no vomiting or convulsions, but the girth of the head was 18 inches. On June 1st the child was admitted to the hospital under the care of Dr. Sansom. The horizontal girth of the head was then  $18\frac{1}{4}$  inches, and all the bones of vertex were

widely separated. The eyeballs were depressed, and the upper lids were occasionally retracted; there was no strabismus. The limbs showed slight rigidity, but could be straightened; Kernig's sign was not present. The temperature was normal. The optic discs appeared blurred, and it seemed probable that the child was blind.

On June 4th lumbar puncture was performed, and Dr. Hunter reported the diplococcus meningitidis to be present.

At the end of a week the child seemed to be getting worse, and vomiting commenced; the mother's desire to take the child home was therefore acceded to.

On June 18th the child was seen at home, and still seemed very ill; there was slight strabismus, some retraction of the head and some rigidity of the limbs, and Kernig's sign was present.

On July 13th she was again seen in the out-patient department, and had greatly improved. The hydrocephalus remained stationary, but there were no signs of meningitis.

On the 19th of April, 1902, she was again seen, and presented the typical appearance of chronic hydrocephalus. The horizontal girth of the head was then  $20\frac{3}{4}$  inches, and the measurement between the auditory meatus  $13\frac{3}{4}$  inches.

CASE 15.—Solomon B—, aged 6 months, admitted April 4th, discharged June 27th, 1901. On admission under Dr. Gilbert Smith it was stated that the child had been ill for three weeks, starting with convulsions, followed by bronchitis and pneumonia, and that during the last few days he had vomited occasionally and had been convulsed. The mother thought that the child had been blind for four days. He was breast-fed, but had had some cow's milk in addition. There was marked retraction of the head, an occasional squint, and intermittent elevation of the upper lids; Kernig's sign was well marked. The fontanelle was patent and bulged.

Lumbar puncture was performed, and a large test-tube



was half filled with clear fluid, in which no micro-organisms were found. The child continued in much the same condition, with marked cervical opisthotonos, Kernig's sign, occasional retraction of upper lids, and strabismus. The temperature remained normal, and vomiting was infrequent. On April 9th lumbar puncture was again performed, two test-tubes full of fluid being removed. In this micro-organisms were found, but no diplococci. Lumbar puncture was repeated on May 17th and on May 27th, 2 oz. of fluid being removed on each occasion, and on June 8th 3½ oz. were taken away. On June 1st it was noted that there was very slight, if any, rigidity of the neck and limbs.

The child seemed happy and smiling; as far as could be determined he was blind. The movements of the hands were rather jerky, and there was still occasional retraction of the upper lids, so that the sclerotics showed above the corneæ. The discs were clear. The child continued in much the same condition, apparently suffering from internal hydrocephalus, which threatened to be chronic when he was sent home owing to the occurrence of scarlet fever in the ward. For the last four weeks before his discharge the temperature had been quite normal, and vomiting had only occurred very seldom.

CASE 16.—Etta S—, aged 1½, admitted May 3rd, discharged May 23rd, 1901. The illness began with convulsions, seven weeks before admission under Dr. Warner. The bowels had been constipated, all food had been vomited, and there seemed to be abdominal pain. The heart, lungs, and abdomen presented no signs of disease. There was very marked retraction of the head, some rigidity of the right arm, but no Kernig's sign. There was no photophobia, no squint, no retraction of the upper lids, no movements of the lower jaw. The fontanelle was closed. The discs appeared normal. The temperature, generally subnormal, occasionally rose for a short time; the highest rise was to 102°. Vomiting occurred only occasionally.

On May 15th the child was found sitting up with no retraction of the head or stiffness of the neck, no rigidity of the arms or legs, and apparently completely recovered.

On admission, lumbar puncture was performed, and the *diplococcus intracellularis meningitidis* was found to be present in pure culture. The child was discharged cured on May 23rd.

CASE 17.—Ellen T—, aged 3 months, admitted March 12th, discharged June 28th, 1901. This child was admitted under the care of Dr. Gilbert Smith on March 12th, with a history that for the past five weeks she had been wasting and that she had had a cough; during the week previous to admission she had had convulsions in her sleep, and for the last few days she had vomited after her food. She had been fed on milk and barley-water.

On admission the child was found to be extremely emaciated, but there was no evidence of thoracic or abdominal disease. There was slight retraction of the head, and Kernig's sign was present; the pupils were equal and reacted to light.

On March 14th lumbar puncture was performed, and in the fluid obtained the *diplococcus meningitidis* was reported to be present. There was also some convergent strabismus.

On March 15th some œdema appeared over the back of the sacrum and extended to the angles of the scapulæ.

On March 22nd the child appeared much wasted, but was not particularly irritable; she took her food well. With the hips flexed to a right angle with the trunk, the knees could not be extended beyond  $135^{\circ}$ . There was no strabismus; no retraction of the upper lids, and the fontanelle appeared natural.

On April 9th there was found to be some retraction of the head, and occasional retraction of the upper lids was noticed for the first time.

On April 12th lumbar puncture was again performed, and the *diplococcus* was reported to be present.

On April 26th the child was better and had gained weight ; there was occasional retraction of the upper lids ; Kernig's sign was present upon the right side, but not upon the left.

On May 6th there was no retraction of the head, but marked occasional retraction of the upper lids. Kernig's sign was not present on either side.

The temperature throughout was subnormal. For the first four days there was occasional vomiting, but subsequently it only occurred at very infrequent intervals. On discharge the child seemed to have recovered almost completely ; it seemed probable that the child was neither deaf nor blind. The weight, which shortly after admission sank to 6 lbs. 14 oz., rose to 8 lbs. 9 oz. on discharge. The intermittent retraction of the upper lids, however, persisted.

On July 6th she was admitted for a few days for convulsions, which, however, were not repeated in the hospital ; no evidence of disease was then found.

CASE 18.—Esther L—, aged 6 months, admitted April 20th, discharged June 27th, 1901. The child on admission under Dr. Gilbert Smith had been ill for five weeks, being very feverish and fretful and vomiting occasionally. The head had been retracted throughout.

On admission the head was retracted and the fontanelle bulged ; Kernig's sign was not present. The knee-jerks were equal and easily obtained. The pupils were equal and reacted to light ; there was no squint. The fundi showed no pathological appearances. There was no evidence of thoracic or abdominal disease.

Lumbar puncture was performed on April 21st, and the fluid was reported to contain the meningococcus. On the following morning it was found that the fontanelle was level and pulsated. The head was markedly retracted, but there was no rigidity of the arms or legs, and Kernig's sign was not present. There was no squint ; the pupils were equal and reacted to light. The eyes were generally

kept open, and there was no photophobia. Occasionally the upper lids were slightly retracted, but not sufficiently to show the sclerotics above the corneæ. The fundi appeared normal. The child took her food well from the bottle, though she had been breast-fed until admission.

On April 26th the child was lying quietly, apparently taking notice of her surroundings. The upper lids were occasionally retracted so as to allow a band of sclerotic to appear above the corneæ; there were occasional dissociated movements of the eyeballs, but there was no permanent squint. The head was slightly retracted. There was no rigidity of the arms and legs, and Kernig's sign was not present. There were no continued movements of the lower jaw.

On May 8th the neck was still rigid, but there was no retraction of the head. The occasional retraction of the upper lids was still present. There was no squint and no rigidity of the legs; the left arm was markedly rigid, and kept closely apposed to the chest.

On June 1st there was but slight rigidity of the neck, and no retraction of the head. The occasional retraction of the upper lids persisted, but there was no squint or dissociated movement of the eyes, and no rigidity of the limbs. The child seemed to be gaining ground, but still had occasional attacks of fever associated with vomiting and malaise. The temperature at first remained at about 99° or 100°, with an occasional rise to 101° or 102°, but the rises became more infrequent, and after about the seventh week in hospital the temperature remained near the normal. Vomiting occurred at intervals throughout the child's stay in hospital, but was never very frequent. She was discharged almost recovered from the meningitis on June 27th owing to an outbreak of scarlet fever in the ward. The weight on admission was 10 lbs. 11 oz., and fell to 9 lbs. 11 oz. during the fourth week, when it began to rise again uninterruptedly, and was 11 lbs. just before discharge.

On July 16th the child was readmitted; she had had

some diarrhoea, but the condition otherwise was not much changed. The head was slightly retracted; there was no rigidity of the arms or legs, and Kernig's sign was not present. There was no squint, but the upper lids were occasionally retracted. The child seemed happy, and the spontaneous movements of the limbs appeared natural; no evidence of cerebral defect could be discovered.

CASE 19.—George P—, aged 5, admitted June 8th, discharged July 4th, 1901. The child on admission under Dr. Sansom had been ill for four or five months; for the past two months his walking had been unsteady, and he had frequently fallen and hurt himself. He had had abdominal pain, and vomited every morning about a pint of watery fluid. His mother and father both died of phthisis about two years ago; there were two other children apparently quite healthy.

On admission the child appeared well nourished and happy, but seemed a little foolish. The horizontal girth of the head was  $22\frac{1}{4}$  inches. The heart rhythm was irregular, the pulse frequency increasing during inspiration. The lungs were free. There was alternating strabismus, but no nystagmus. The left pupil was larger than the right, and both reacted to light and with accommodation. There was no apparent blindness or deafness; the tongue was protruded in the middle line, and there was no facial paralysis or speech defect. There was marked double optic neuritis.

During examination he was seized with a sudden attack of pain referred behind the left ear, which made him weep copiously. The gait was very staggering, but there was no marked tendency to fall in one direction. The knee-jerks were obtained with great difficulty; the plantar reflex was of the flexor type on the right side, and was not obtained upon the left side. The right cremasteric reflex was present, but not the left. Later the knee-jerks were not obtained. Kernig's sign was not present; in fact, there seemed evidence of some hypotonus in the legs.

On June 10th lumbar puncture was performed, and Dr. Hunter reported the presence of Weichselbaum's diplococcus in the fluid.

On June 12th the boy vomited a round worm. There was no headache, but the vomiting was frequent; the swelling of the optic discs continued, and there was a definite squint. There was no rigidity of the limbs or neck.

On June 17th there had been no vomiting since the 12th, the squint persisted, and the patient complained of pain behind the left ear.

On June 24th the temperature, which had been normal, rose to  $100^{\circ}$ , and on the 27th a definite measles rash appeared. The measles ran a normal course, and on July 4th the boy was discharged apparently relieved of all his symptoms.

CASE 20.—John E—, aged  $1\frac{1}{2}$  years, admitted July 6th, 1901, discharged August 30th, 1901. The illness began on September 29th with diarrhoea and vomiting. He was brought to the out-patient department on July 2nd, and was then found to have some bronchitis; he was treated as an out-patient until July 6th, when, as no improvement was manifested, he was admitted under Dr. Schorstein.

There was no history of tuberculosis in the family.

On admission the temperature was  $100.2^{\circ}$ , and there was some general bronchitis. The diarrhoea was urgent, but there was no vomiting during the first week. Two days later there was noticed marked retraction of the head. This continued, and on July 12th the child began to vomit. On July 15th lumbar puncture was performed, and Dr. Hunter reported the fluid to contain the diplococcus intracellularis in pure culture. On July 19th the child was drowsy and apathetic; there was some rigidity of the neck, but no retraction of the head. The pupils were equal and reacted to light; apparently the patient was not blind. There was no squint, no retraction of the upper lids, Kernig's sign was not present, and the limbs

were not rigid. Vomiting continued at intervals from July 12th to July 21st, and then became infrequent. The temperature during this time rose to  $100^{\circ}$  each evening, but subsequently was normal.

From this time the child progressed satisfactorily, and on discharge seemed to have completely recovered. The fundi were examined on several occasions, and were never found to present any pathological appearances.

CASE 21.—Albert P—, aged 3 years, admitted September 5th, 1901, discharged October 11th, 1901. The illness commenced on September 1st with vomiting and "screaming" fits, which were followed by stupor. There was a history of tuberculosis in the mother's family, and one other child had meningitis, from which she had recovered (Maria P—, in Great Ormond Street, in March, 1893).

On admission under Dr. Warner the child seemed stupid; he was very irritable, and screamed when disturbed. There was marked head retraction, and an intermittent strabismus of the right eye. On September 11th the head retraction persisted, and Kernig's sign was present in both legs, but there was no other rigidity of the limbs. There was no sign of thoracic or abdominal disease. He could see and hear, and understood questions. He complained of pain at the back of the head. There was still an intermittent strabismus. On September 14th lumbar puncture was performed, but no fluid was obtained; later the operation was repeated with success, and  $2\frac{1}{2}$  ounces of fluid obtained. Dr. Hunter reported the presence of the diplococcus intracellularis in pure culture. On September 21st the retraction of the head continued, but the child seemed better. On October 7th there was no retraction of the head, but some slight rigidity of the neck. He was not very bright, but otherwise seemed quite well. On Nov. 2nd he was discharged apparently completely recovered. For the first eighteen days the temperature was irregular, ranging from  $98^{\circ}$  to  $101.4^{\circ}$ , but subsequently was about normal. Vomiting was never

very frequent, but occurred at intervals during the first four weeks.

CASE 22.—John C—, aged 3 years, admitted October 13th, 1901, discharged November 4th, 1901. Three weeks before admission under Dr. Gilbert Smith the child fell out of a barrow and hurt the back of his head. Since this accident he had been irritable and refused his food, becoming delirious at night. For the past week there had been diarrhoea, but there had been no vomiting. There were dissociated movements of the eyeballs, but no definite rigidity of the neck or retraction of the head. Kernig's sign was not obtained. Lumbar puncture was performed, and six drachms of fluid removed, in which Dr. Hunter found the diplococcus meningitidis. The temperature on admission was 100°, but subsequently, with the exception of one evening, was normal or subnormal. Vomiting occurred occasionally for the first eight days, but not subsequently.

For nearly three weeks the child uttered no sound, but apparently could both see and hear. He was discharged on November 4th to attend as a ward out-patient, being still very irritable but able to speak. Since his discharge he has gradually improved, and is now apparently restored to his normal health.

CASE 23.—Elizabeth S—, aged 6, admitted March 8th, 1901, died March 13th, 1901. The child was brought to the out-patient department on March 5th, with the history that she had fallen downstairs ten days before and had hurt her back. For the last five days there had been headache and vomiting. The temperature was 101°, but no physical signs of disease could be discovered; she was sent home to bed, to be brought up again on the following day, when no change in the condition was found.

On the morning of the 8th she had a fit, was brought to the hospital, and admitted under Dr. Warner.

There seemed to be no evidence of thoracic or abdo-



minal disease; the temperature was  $99.6^{\circ}$ . She was unconscious, and lay still save for a rhythmic movement of left hand and forearm, and occasional movement of the jaw as if in mastication. The pupils were widely dilated and fixed, and there was no photophobia. There was slight lateral nystagmus and slight left internal strabismus. There was no rigidity of the neck, but Kernig's sign was present. There was incontinence of urine. Knee-jerks were not obtained.

In the evening lumbar puncture was performed, and about two ounces of clear fluid removed, which proved to contain the meningococcus. On March 11th it was noted that there was slight ptosis of the right lid, and some dissociated movements of the eyeballs, with right internal strabismus. Occasionally she called for her mother, but did not seem to recognise her. There were no twitchings and no marked rigidities. The right pupil was dilated and fixed; the left pupil was smaller and reacted to light. Incontinence persisted. On March 13th there was some rigidity of the neck, but Kernig's sign was not present. Wasting had been very rapid. An ulcer had developed upon the right cornea. Dissociated movements of the eyeballs were noted. The discs were examined several times, but no definite changes were noted. The temperature ranged from  $99^{\circ}$  to  $101^{\circ}$  until just before death, when it rose to  $102.4^{\circ}$ . There was no vomiting while she was in the hospital.

The urine once contained a trace of albumen, but, tested again, it was normal.

*Post-mortem examination.*—A caseating bronchial gland was found, from which tuberculous infection had spread to visceral pericardium; there was, however, no acute pericarditis.

No evidence of tuberculosis could be found elsewhere.

There was some excess of fluid at the base of the brain and in the spinal theca and in the ventricles; also some purulent lymph was found in the interpeduncular space, on the under surface of the cerebellum, and down the spinal cord.

The brain substance and the pia mater appeared congested.

CASE 24.—Bella C—, aged 1 month, admitted and died March 11th, 1901. A seven-months child, one month old, was admitted under Dr. Percy Kidd on March 11th, with the history that she had been suffering from convulsions for one day. There was slight retraction of the head, but no strabismus; the convulsions continued, affecting both arms and legs, and shortly after admission she died.

At the post-mortem examination all the organs appeared healthy except the brain, which showed acute suppurative vertical meningitis. The diplococcus intracellularis and pyogenic organisms were found by Dr. Hunter to be present in the lymph.

CASE 25.—Michael G—, aged 4 months, admitted April 4th, 1901, died April 10th, 1901. The child was breast-fed, and was quite well until April 2nd, when he had a fit; on the 3rd there were nine fits, and on the 4th there had been six before admission to the hospital under Dr. Gilbert Smith. During the day of admission there were seven more fits, but they then ceased. The fits consisted of general clonic convulsions, the pupils being dilated and immovable, and the eyes turned to the left. In the intervals between the fits the pupils were equal and contracted, and reacted to light. There was no retraction of the head or rigidity of the body, and Kernig's sign was not present; the temperature ranged between 97° and 99°, and there were no physical signs of thoracic or abdominal disease.

On April 5th the child appeared perfectly well, and continued so; on April 7th he was allowed to be taken home, so that the mother might resume nursing.

On April 9th he was again brought to the hospital, because for thirty hours he had taken nothing; there had been no fits in the interval. The child took the bottle

well in the hospital, and the notes state that there was no bulging of the fontanelle, no squint, and no changes in the fundi. The pupils were large, equal, and reacted to light. The neck was slightly rigid, but there was no retraction of the head; the knee-joints could not be completely extended with the hips flexed, but there was no definite Kernig's sign. The knee-jerks and plantar reflexes were present. No signs of thoracic or abdominal disease could be found. The temperature was  $98^{\circ}$ . On the following day the temperature rose to  $100^{\circ}$ , and the child became convulsed, and died.

At the post-mortem no naked-eye pathological appearances were found. There was no evidence of meningitis, and no excess of cerebro-spinal fluid. The diplococcus intracellularis and pyogenic organisms were found in the fluid by Dr. Hunter.

CASE 26.—Samuel G—, aged 15 years, tailor. This boy had been ill in bed for three weeks before admission under Dr. Gilbert Smith. The illness commenced with a violent headache, which had persisted; there had been no vomiting; his mind had been clear until the last twenty-four hours, during which he had been delirious and had not recognised his relatives. He had been deaf for five years, and had had double otorrhœa for that time until the onset of the present illness, when the discharge ceased.

On admission he screamed when touched anywhere, and lay with his legs drawn up, and Kernig's sign was present. The neck was rigid, but there was no retraction of the head. The pupils were equal, and reacted to light. There was no otorrhœa, but both membranes were perforated; there was no œdema or tenderness over the mastoids; there was no squint. The knee-jerks were present and equal. Both fundi appeared normal. There was retention of urine.

On April 4th paresis of the right side of the face and of the right arm was noticed; the condition otherwise was unchanged, save that he seemed more drowsy. He was

then transferred to the surgeon. The temperature for these three days was about  $99.4^{\circ}$ , and there was no vomiting. Mastoidectomy upon the left side was performed, but no pus was found; a trephine hole was made over the left temporo-sphenoidal lobe and this region of the brain, and later the cerebellum was explored. The membranes bulged into the trephine hole, but no pus was found on further exploration. On the following day he seemed slightly better; the facial paresis was less marked; the temperature, however, rose to  $101^{\circ}$ . On the third day the left pupil was noticed to be larger than the right, and there was some ptosis on the left side, and a little difficulty in swallowing. These signs increased, and complete paralysis of the palate developed. During the last twenty-four hours the breathing became periodic. Death was somewhat sudden.

At the post-mortem examination there was found to be some broncho-pneumonia in the left lung. The cerebral ventricles were distended and the convolutions flattened; there was a large quantity of clear fluid at the base of the brain.

Dr. Hunter reported the fluid to contain the meningococcus in large quantities, and also pyogenic organisms. There was no lymph seen, and no evidence of tuberculosis. The site of the mastoidectomy was healthy, and also the petrous bones. Both middle ears contained pus.

CASE 27.—Isaac M—, aged 19 years, carman, admitted May 7th, 1901, died May 14th, 1901. This man had been quite well until the day before admission under Dr. Gilbert Smith, when he had been suddenly attacked by headache, drowsiness, vomiting, and diarrhoea, with stiffness of jaws.

On admission he was in a semi-comatose, irritable state, resenting interference forcibly, and making no reply to questions; he apparently, however, did not resent a hard pin-prick any more than a light touch. He lay upon his left side, huddled up, and did not move unless disturbed. The neck was rigid and the head a little retracted; the

pupils were dilated and fixed. There was no strabismus. The fundi showed no pathological changes. There were no signs of paralysis of face or limb, no signs of mastoiditis, no tenderness over the occiput or spine, and no evidence of thoracic or abdominal disease. The legs were rigid, but Kernig's sign was not obtained; the knee-jerks were obtained on both sides, and Babinski's phenomenon was present. The temperature was  $100.4^{\circ}$ . On May 8th a catheter was passed in consequence of retention of urine, and 20 oz. were withdrawn. He became very violent and needed shackling, but quieted down and slept for half an hour after an injection of morphia; he was very restless afterwards, constantly calling for his friends. He took his milk fairly well through the day, but had incontinence of urine. In the evening the pupils were equal and reacted to light. He passed a fairly quiet night, but became noisy on the morning of the 9th; there was then a divergent strabismus, but in other respects his condition was unchanged. He slept under the influence of morphia. On May 10th the pupils were equal and reacted to light, but there was no fear reflex, and it seemed probable that he was blind. There was considerable retraction of the head, and attempts at flexion caused him to call out: "Oh! my head and neck." There was no strabismus, and the fundi appeared normal. A patch of herpes appeared upon the right cheek; there was marked distension of the abdomen; incontinence of fæces as well as urine set in. In the evening signs of congestion of the bases of the lungs developed. On May 11th the condition of noisy delirium still persisted; the knee-jerks were not obtained, and Kernig's sign was present. In other respects his condition remained almost unchanged. On the 12th and 13th he gradually became quieter, and developed some signs of consolidation at the base of the right lung. The temperature on admission was  $100.2^{\circ}$ , and rose to  $103^{\circ}$  on the following morning; then it fell to  $99^{\circ}$  for three days, rising to  $103^{\circ}$  on May 11th, gradually falling to  $100^{\circ}$  on the morning of May 14th, just before death. While in

hospital he vomited three times, and except just at first there was complete incontinence of both urine and fæces.

At the post-mortem examination there was found to be pneumonia at both apices in a stage approaching grey hepatisation; there was also some consolidation at the left base. The brain showed some streaks of purulent matter over the vertex; the membranes at the base were milky, and there was some definite pus on the under surface of the cerebellum. There was no excess of fluid in the ventricles, except that there was some pus in the fourth ventricle. The brain substance, though, appeared pinker than normal. Purulent inflammation extended down the whole length of the cord.

Dr. Hunter reported the presence of the diplococcus intracellularis meningitidis and of the pneumococcus in the cerebro-spinal fluid.

CASE 28.—Jessie B—, aged 1 year and 3 months, admitted May 7th, 1901, died May 23rd, 1901. The child had been bottle-fed since birth, and had been healthy, save for one fit when three months old, until a week before admission under Dr. Gilbert Smith, when she had another fit. She had screamed a great deal since, and though she had had no recurrence of the convulsions the mother said that “she went stiff when touched.”

On admission the temperature was  $100^{\circ}$ , and it rose to  $102^{\circ}$  on the following morning. There were signs of general bronchitis. The fontanelle was patent and bulging; there was retraction of the head. The pupils were equal and reacted to light; it was doubtful if there was some strabismus. There was no retraction of the upper lids. The knee-jerks were not obtained, and Kernig's sign was not present. Lumbar puncture was performed, and the fluid was reported to contain the pneumococcus and diplococcus intracellularis. On May 9th, after lumbar puncture, the fontanelle was noticed to pulsate; the head was markedly retracted, but there was no rigidity of the limbs, and Kernig's sign was not

present. The bronchitis persisted and the cough was frequent; the child yawned often; there was no squint, and no retraction of the upper lids. On May 11th the fontanelle was found to be bulging but pulsating; the head was markedly retracted, but there was no rigidity of the limbs, and Kernig's sign was not present. There was no squint and no retraction of the upper lids. The optic discs appeared blurred on admission, and subsequent notes reassert this, but there was no definite evidence of optic neuritis. The temperature continued between  $100^{\circ}$  and  $102^{\circ}$ , with only two intermissions, until forty-eight hours before death, when it fell to  $99^{\circ}$  and continued there. For the last nine days of life vomiting was frequent, but had not occurred in the earlier part of the illness.

The post-mortem examination showed general bronchopneumonia. There was purulent meningitis limited to the basal subarachnoid cistern and under surface of cerebellum, and spreading all down the cord. There was no excess of fluid in the ventricles.

CASE 29.—Abraham D—, aged 2 years and 10 months, was admitted to the London Hospital on January 30th, 1901, under the care of Dr. Stephen Mackenzie, with the history that he had been ill for two months with fever, irritability, and attacks of cramp, with marked wasting. He had been fed on milk and beef tea since the commencement of the illness; there had been no vomiting; the bowels had only acted after medicine. The only previous illness was measles eighteen months before. The child was found to be irritable, with a puny cry; the head was rigidly retracted. There was no discharge from the ears; the pupils were dilated, equal, and reacted to light. There was no optic neuritis. The knee-jerks were increased; the plantar reflexes were normal, the toes moving down. There was no rigidity of the legs either with the hips extended or flexed to a right angle. Everything was passed under him. He continued in the same condition until February 10th, when vomiting set in and

continued almost daily until his death. On February 21st some internal strabismus was noted, and occasional retraction of the upper lids, showing the sclerotic above the cornea. The retraction of the head continued; there was no Kernig's sign. Definite optic neuritis developed. Wasting became more obvious. On February 26th lumbar puncture was performed. The fluid obtained proved to contain diplococci meningitidis and probably bacillus influenzae. The wasting increased, and he died from exhaustion on March 4th.

On admission the child weighed 19 lbs. 6 oz.; at first he gained a few ounces, but when the vomiting commenced he began to lose weight, and a week before death weighed only 18½ lbs. The duration of the illness was three months. The temperature, as a rule, was subnormal; once, three days before death, it rose for a few hours to 102·8°.

At the post-mortem examination there was found much internal hydrocephalus, with opacity of the arachnoid at the base, but with no other evidence of acute meningitis. There was no sign of tuberculosis.

CASE 30.—Edwin Thomas R—, aged 4½ months, admitted March 3rd, 1901, died May 31st, 1901.

On admission under Dr. Sansom the child had been ill for five weeks, and had had frequent convulsions. He had been fed at the breast; both mother and father were healthy. He was very irritable, and the head was markedly retracted.

On March 7th occasional retraction of the upper lids was noticed. On March 12th the head was still rigidly retracted, the fontanelle was found to be bulging, and there was occasional retraction of the upper lids. There was no rigidity of the limbs, and Kernig's sign was not present. There had been no convulsions since admission, and the child had taken his food fairly well, though there was occasional vomiting. The weight had decreased from 11 lbs. 6 oz. to 10 lbs. 10 oz. The fundi appeared normal.



The child continued in much the same condition, occasionally appearing to improve slightly and at other times appearing worse. It appeared that the child was blind, but no changes in the fundi were noted at any time. Kernig's sign was never present, but occasionally there seemed to be some slight rigidity of one arm.

Vomiting was infrequent after the first fortnight until a week before death, when it recommenced with some diarrhoea. The retraction of the head persisted throughout, and the occasional drawing back of the upper lids also continued. No strabismus was noted at any time. The temperature was normal or subnormal throughout, except on three occasions, when for a few hours it rose to  $100^{\circ}$  or  $101^{\circ}$ . Just before death the child weighed 9 lbs. 4 oz. Lumbar puncture was performed on March 12th, and the diplococcus intracellularis found present with another bacillus, resembling the bacillus influenzae. The total duration of the illness was eighteen weeks. At the post-mortem examination all the organs except the brain were found to be healthy. The ventricles were enormously distended with fluid, and there was much fluid in the spinal theca. There was some milkiess of the membranes at the base, but no lymph was found anywhere.

CASE 31.—Harry K—, aged 1 year, admitted February 28th, discharged July 12th, 1901. The child had been well until 10.30 p.m. on the day before admission under Dr. Gilbert Smith, when he became feverish and vomited. He had been breast-fed until admission, but occasionally had had a little cow's milk. There were signs of broncho-pneumonia with evidence of consolidation at the right apex. The temperature was  $104.6^{\circ}$ .

On March 7th a squint was noticed, and it was thought that there was some retraction of the head; the hands twitched occasionally. The body generally was somewhat rigid. The knee-jerks were not obtained. The signs of broncho-pneumonia had disappeared. On March 11th he vomited once; on the 14th there was marked retraction

of the head, and Kernig's sign was present; the knee-jerks were obtained. On March 15th lumbar puncture was performed, and the fluid was reported to contain the *diplococcus intracellularis meningitidis*. On the following day the notes say that the fontanelle was depressed; there was double internal strabismus; the pupils were equal and of medium size, and reacted to light. There was no rigidity of hands or arms or of neck; there seemed to be no definite evidence of Kernig's sign, though there was some resistance to complete extension of the knee-joints when the hips were flexed. There was no retraction of the upper lids. The child seemed to be getting much thinner, though he took his food well. The fundi showed no apparent pathological change.

On March 22nd the fontanelle was depressed; there was right internal strabismus, occasional retraction of the upper lids, and marked retraction of the head. There was some rigidity of the shoulders, and Kernig's sign was present. Since the 20th vomiting had been frequent, and he had taken his food badly. The fundi appeared normal. On March 27th the retraction of the head was still very marked, and the wasting was pronounced. There was no rigidity of the limbs, and Kernig's sign was not present. The pupils were equal, and there was right internal strabismus; the jaw was frequently moved as if in mastication. The vomiting continued, but for the last two days he had taken his food better.

On April 3rd the head was markedly retracted, and the limbs were kept flexed. The wasting continued, but since the 30th vomiting had been infrequent. The movements of the lower jaw were very marked; the squint persisted. The child lay half asleep, crying very little. The eyes were sometimes closed and sometimes open; occasionally the upper lids were retracted, so that the sclerotics showed above the corneæ. The fundi appeared normal.

On April 16th the emaciation was extreme, and the retraction of the head very marked; the lower jaw was constantly moving as if in mastication. The eyes were

kept open and the eyeballs were depressed, and retraction of the upper lids was very frequent. There was some rigidity of the legs, but Kernig's sign was not definitely present.

On April 20th the child seemed in much the same condition. There had been no vomiting since April 9th.

On May 1st the child seemed much better; he was very fretful if disturbed, and moved his limbs freely and spontaneously.

On May 3rd it was noted that the child looked fatter, and had gained 2 lbs. in weight in the past week. He seemed more fretful. There was depression of the eyeballs, with occasional retraction of the upper lids. The squint was still present, and also the frequent movements of the lower jaw. The girth of the head was 19 inches, an increase of half an inch since the last measurement on April 18th.

On May 9th and subsequently the girth of the head was 19½ inches. From this time the child seemed steadily to gain ground so far as his general health was concerned, but he gradually got into a condition in which he lay upon his back all day kicking and throwing his arms about, and laughing in a manner suggesting a condition of idiocy. The depression of the eyeballs continued, and there developed a kind of coarse nystagmus or intermittent squint. The optic discs appeared whiter than normal; it was not thought, however, that the child was blind.

The temperature, which was 104.6° on admission, when there was broncho-pneumonia, fell two days later to 97.2°; after this it was irregular, varying between 97° and 103° for ten days, and then irregular with slighter variations for four more weeks, after which it was normal. The vomiting began on March 11th, and continued to be severe until April 29th, after which it was much less frequent and soon ceased.

On April 15th, when the emaciation was most extreme, the child weighed 13 lbs.; on discharge his weight was 1 st. 7 lbs.

Seen on December 3rd, 1901, the child was well nourished and happy; could walk well, though he carried his head tilted a little to the left. He could see and hear well. He could not be got to speak, however. Girth of head, 19½ inches. The child did not appear to be an idiot, or much below the normal mental development for his age.

CASE 32.—William A—, aged 3 years, admitted September 17th, died September 28th, 1901. This child was admitted under the care of Dr. Percy Kidd, with the history that he had been vomiting frequently for the past fortnight. A squint had been noticed for one day; no retraction of the head or twitching of the limbs had been noticed.

On admission there was no rigidity of the neck, and Kernig's sign was not present; the child resented disturbance. There was some dissociated movements of the eyeballs, producing an occasional squint. The pupils were small, and the left was slightly larger than the right.

On September 20th there was some rigidity of the neck. On September 22nd lumbar puncture was performed, and from the fluid thus obtained Dr. Hunter isolated the *diplococcus intracellularis*.

For the first week in hospital the temperature was normal; it then rose, and remained between 99° and 101° until death on September 28th. There was no vomiting in the hospital. The duration of the illness was twenty-seven days.

At the post-mortem examination there was found some broncho-pneumonia at the base of the right lung, and a caseating bronchial gland. The other viscera appeared healthy. There was much purulent lymph at the base of the brain and on the under surface of the cerebellum; the convolutions were matted together. Tubercles were found along the vessels. The ventricles were distended with fluid, and in them was found some floating lymph. The vertex appeared normal save for the flattening of the convolutions.

CASE 33.—William W—, aged 1 year 9 months, admitted March 13th, died March 17th, 1901. The child was first brought to the out-patient department on July 22nd, 1899, when three months old, and was then found to be suffering from congenital syphilis; there was a nasal discharge and the hot-cross-bun deformity of the skull. Up to that time he had been breast-fed, and was ordered to be given the bottle in addition. The child was under treatment until March, 1900, showing considerable improvement. Attendance was then discontinued until December 19th, 1900, when the child was again brought up with a history of irritability and retraction of the head; it seemed possible that the child had tuberculous meningitis. He was brought up again twice and improved, ceasing attendance on January 16th. On March 13th he was again brought up, having had a convulsion; there was then retraction of the head and strabismus; the temperature was  $99^{\circ}$ . He was admitted under the care of Dr. Percy Kidd. Shortly after admission he again became convulsed, both arms and the right leg being rigid and the left leg showing clonic movements. The eyes were turned to the left and there was no strabismus. Kernig's sign was present on both sides. No definite changes in the fundi were observed. Lumbar puncture was performed, and half a test-tubeful of clear fluid was removed. After this the convulsions ceased. On March 15th rigidity of the neck was noticed, with bulging of the fontanelle; there was no squint and no rigidity of the limbs; Kernig's sign was not present. There was no retraction of the upper lids.

On March 16th retraction of the head was marked, and there was difficulty in swallowing. Kernig's sign was present upon the right side only.

The temperature was  $97^{\circ}$  on admission, and rose to  $101.8^{\circ}$  on March 15th, falling to  $99^{\circ}$  on the 16th, thence rising rapidly to  $108^{\circ}$  just before death, on the morning of the 17th.

At the post-mortem examination there was found acute

miliary tuberculosis of all organs, with basal tuberculous meningitis.

CASE 34.—Ethel G—, aged 3½ years, admitted April 15th, died April 19th, 1901. This child was first brought to the out-patient department on April 10th, with the complaint that she had been vomiting all food for the past five days. The bowels had not acted for two days, and there was headache. The temperature was 99·4°. The abdomen was a little retracted, but there were no definite physical signs of disease. The knee-jerks were obtained. Three days later the child was seen again. The temperature was 101°, the vomiting and headache continued, and the bowels had not acted. There was no retraction of the head, and Kernig's sign was not present; the knee-jerks were not obtained. On April 15th she was brought up again, and it was found that a squint had developed; the knee-jerks were not obtained, and there was some rigidity of the neck. The headache had persisted, and she had vomited once each day. She was admitted to the hospital under Dr. Percy Kidd. In the ward the temperature was 101·2°, and it was noted that there was an intermittent squint. Kernig's sign was not definite. On the following morning it was noted that the child lay usually with her eyes open, but that she could close them. The left pupil was larger than the right; both reacted to light; there were dissociated movements of the eyeballs, but no retraction of the upper lids. The neck was rigid, but there was no retraction of the head; the limbs were kept in the attitude of flexion, and she resisted attempts to straighten them, but Kernig's sign was not definitely present. Passive movements of the limbs seemed to cause pain. The fundi appeared normal; she was not blind, and there was no photophobia. On April 18th the child was much worse, being quite unconscious. Kernig's sign was definitely present in both legs. There were continued irregular movements of the arms and legs without any tendency to repetition, and more marked on the left side.

The neck was rigid, but there was no retraction of the head. There was no retraction of the upper lids. On April 19th it was noted that there were frequent dissociated movements of the eyeballs, with a kind of coarse nystagmus in the left eye, apparently produced by frequent contractions of the left internal rectus. The child seemed to be blind, and the fear reflex was absent. The right pupil was larger than the left, and neither reacted to light. There was no retraction of the lids; Kernig's sign was not present; the neck was rigid, but the head was not retracted. The knee-jerks were not obtained, possibly owing to the rigidity of the legs. There was considerable resistance to passive movement in all the limbs. The arms both carried out large, slow, irregular movements, without any tendency to a repetitive cycle. These movements were most marked in the left arm; the left leg also performed slight, irregular, slow, large movements. The note says that the movements were choreic in type, but were apparently modified by the rigidity of the limbs. The distribution was mainly hemiplegic. Lumbar puncture was performed on April 16th, and two test-tubes filled with clear fluid; there was apparently no amelioration of the symptoms. The temperature on admission was  $101.2^{\circ}$ , and rose to  $102.9^{\circ}$  just before death on the evening of April 19th. There was no vomiting in the hospital.

At the post-mortem examination there was found miliary tuberculosis of the lungs and spleen, with a caseous bronchial gland. There was much lymph at the base of the brain, and many tubercles were seen in the Sylvian fissures. There was an excess of fluid in the spinal theca, but no lymph; there was a slight excess of fluid in the ventricles.

CASE 35.—Charles F—, aged 6 months, admitted April 16th, died April 21st, 1901. The child had been taken ill on April 8th with vomiting and restlessness; on the day of admission under Dr. Warner he had three

fits, which, according to his mother's account, were stronger on the right side. The child was breast-fed. The face was flushed, the head markedly retracted, and there were general twitchings of all the muscles of the body. The knee-jerks were present and equal. Kernig's sign was not obtained. The fontanelle bulged, but, on lumbar puncture, no fluid escaped. There were signs of general bronchitis.

On April 17th there was marked opisthotonos, the eyes were kept open, and there was occasional retraction of both upper lids, showing the sclerotics above the corneæ. There were dissociated movements of the eyeballs, but there was no persisting squint. The pupils were widely dilated and fixed. There was no photophobia, and the fundi appeared normal. The fontanelle bulged, and no pulsation was felt. There was no rigidity of the limbs, and Kernig's sign was not present. The knee-jerks were readily obtained. The breathing was periodic; at the end of each apnoeic interval there was a spasmodic extension movement of all the extremities. There was no cyanosis.

On April 18th nasal feeding had to be commenced. On the 20th there were frequent convulsive seizures, the head and eyes being turned to the right, with movements of the extremities, which were more marked upon the right side. In the intervals there were constant clonic movements of the eyes to the right, producing a kind of coarse nystagmus. There was rigidity of the neck, but no retraction of the head; the arms were rigid, especially the right. Kernig's sign was obtained. The temperature on admission was  $99.2^{\circ}$ , and remained between  $100.2^{\circ}$  and normal until just before death, when it rose to  $102.4^{\circ}$ . There was frequent vomiting while the child was in the hospital.

Lumbar puncture was repeated on April 18th, and in the fluid obtained Dr. Hunter reported the presence of *Diplococcus intracellularis meningitidis* with other bacilli.

At the post-mortem examination a caseous bronchial



gland was found, and there was miliary tuberculosis of the lungs and spleen. There was much lymph at the base of the brain, and many tubercles were found both in the Sylvian fissures and down the spinal cord. The ventricles were distended with fluid.

CASE 36.—John B—, aged 3, admitted April 20th, died April 28th, 1901. On admission under Dr. Gilbert Smith the child had been ill for two weeks with a bad cough, feverish, and loss of appetite; there had been diarrhoea, but no vomiting. There was no history of tuberculosis in the family. The temperature was  $101^{\circ}$ .

On April 22nd the child appeared drowsy, sleeping with his eyes shut and taking notice of nothing save actual disturbance, which he resented. Passive movement of the limbs was resented and seemed to cause pain; Kernig's sign was not present. There was no retraction of the head and no squint; the pupils were equal and reacted to light; the fundi were normal. Vomiting was frequent, and he took his food badly. There were no signs of thoracic or pulmonary disease.

On April 23rd the neck was rigid, but the head was not retracted; the pupils reacted sluggishly to light, and the left was larger than the right. The legs were stiff, but Kernig's sign was not present; the knee-jerks were not obtained.

On April 26th the child was in a comatose condition, in no wise resenting interference; there was a blotchy, purplish flush upon the face. The left eye was closed and the right open; the left pupil was dilated and fixed; the right was smaller and reacted to light. There was marked rigidity of the right arm and hand, with all the joints fully flexed. The joints of the left arm were also flexed, but were not so rigid. The left hip and knee were flexed, and the ankle extended with considerable rigidity; Kernig's sign was obtained upon the left side. Nasal feeding was necessary.

Lumbar puncture was performed on April 27th, and

half an ounce of fluid was obtained, in which the *diplococcus intracellularis meningitidis* was found by Dr. Hunter.

The temperature was  $101^{\circ}$  on admission, and remained at about  $101^{\circ}$  until just before death, when it rose to  $104.2^{\circ}$ .

At the post-mortem examination there were found caseous bronchial glands and miliary tubercles in lungs and spleen. At the base of the brain there was much greenish lymph, with numerous miliary tubercles. There were no tubercles on the cord. The ventricles and spinal theca were distended with clear fluid, and there was much clear fluid in the basal arachnoid cistern.

CASE 37.—Lily G—, aged 10 months, admitted April 3rd, died April 13th, 1901. The child, who was breast-fed, seemed healthy until March 24th, when she had an attack of vomiting with some diarrhoea, which lasted for three days. On March 30th a squint was noticed, and her mother said that the eyes “rolled about.” She became drowsy and screamed at times. She was brought to the hospital on April 3rd, and admitted under Dr. Gilbert Smith. The neck was then rigid, but there was no retraction of the head; the fontanelle was not bulging. There was a squint. The pupils were equal and reacted to light; the fundi appeared normal. Kernig’s sign was not present; the knee-jerks were equal and increased.

On April 9th nasal feeding had to be commenced, but the child vomited after each feed. There was no retraction of the head, and the fontanelle was slightly depressed; there was some strabismus. The limbs were not rigid, and Kernig’s sign was not present. There was no retraction of the upper lids.

On April 10th lumbar puncture was performed, and 3 oz. of clear fluid removed, and was reported to contain the meningococcus. After the lumbar puncture there seemed to be definite improvement, which, however, only lasted for a short time, and in about forty-eight hours she seemed to be worse again.

On April 12th the left pupil was larger than the right,

and neither reacted to light. The child lay taking notice of nothing, and not resisting disturbance in any way.

The temperature on admission was  $99.8^{\circ}$ ; it continued to be irregular between  $97^{\circ}$  and  $99.4^{\circ}$  until just before death, when it fell to  $96.6^{\circ}$ . Vomiting continued throughout, and towards the end there was some diarrhoea.

At the post-mortem examination caseating bronchial glands, tuberculous broncho-pneumonia, and miliary tuberculosis of the spleen were found. The membranes at the base of the brain were thickened and studded with miliary tubercles. There was no excess of fluid in the lateral ventricles, the walls of which were slightly roughened with a thin layer of lymph.

CASE 38.—Ellen H—, aged 5, admitted June 17th, died June 27th, 1901. The child was brought to the outpatient department on June 13th, with the history that she had felt "tired" for the last fortnight, and that she had felt worse for five days, and had got a headache. She had vomited once on June 12th, and there had been constipation for three days. The temperature was  $100^{\circ}$ . There was not then found to be evidence of organic disease, and she was sent home with an aperient mixture, to come again in four days. When she returned the temperature was  $101.4^{\circ}$ , and she seemed worse and was consequently admitted into the hospital under Dr. Gilbert Smith.

On admission, beyond the fever and the wasting there were no physical signs of disease. The fundi were normal. On the following day it was noted that the child was very irritable and complained of headache; the neck was rigid, but the head was not retracted; Kernig's sign was obtained on the left side only. Lumbar puncture was performed, and  $3\frac{1}{2}$  oz. of clear fluid removed, which proved to be sterile. The withdrawal of the fluid seemed to give immediate relief; the irritability ceased, and the child went to sleep while the fluid was still draining.

On June 19th the child seemed drowsy; the upper lids drooped, and there was a definite squint; the tongue was

foul and there were sordes on the lips. Taches bleuâtres were found scattered over the trunk. Kernig's sign was definitely present on both sides.

On June 21st the child was still drowsy; she was irritable when disturbed, and cried out at times, "My poor head." The neck was rigid; the pupils were dilated and their reaction to light doubtful. There was a definite squint; Kernig's sign was present on both sides; the kneejerks were not obtained.

On June 25th it was noted that the child seemed worse; she rolled her head from side to side, and there were irrelative movements of the arms. The eyes were kept open, and occasionally the upper lids were retracted. Dissociated movements of the eyeballs were noticed, and the child was apparently blind. The neck was still rigid, but there was no retraction of the head. The fundi appeared normal. The temperature remained between 100° and 101° for a week, and then sank to normal, continuing so (with one slight rise) until death on June 26th.

The post-mortem examination showed acute miliary tuberculosis with tuberculous meningitis.

## APPENDIX II.

This case is recorded separately as an example of chronic hydrocephalus sequent upon acute meningitis. It was not included with the other cases because the presence of pulmonary tuberculosis might conceivably invalidate any deductions drawn from a list in which it was included.

*A case of simple meningitis with pulmonary tuberculosis.*—Henry W. P—, aged 8 months, admitted February 6th, 1902, died March 19th, 1902. This child, one of twins, was admitted under the care of Dr. Sansom with the history that he had been wasting for four months, and that for three months the head had been increasing in size. For the first month he had been breast-fed. The other twin died when four months old. Two relations on the mother's side had suffered from hydrocephalus; one

died at the age of ten; the other is still living, and is aged twenty. The child, except for the size of the head, seemed fairly healthy and happy; both anterior and posterior fontanelles were widely patent and bulging. The measurements of the head were: occipito-glabellar, 12 inches; transverse (ear to ear), 12·5 inches; circumference, 18 inches. The heart and lungs appeared normal. For the first fortnight the temperature remained normal. On admission lumbar puncture was performed, and from it Dr. Ainley Walker isolated a diplococcus which he considered to be identical with that described by Weichselbaum, both in morphological and cultural reactions. A week later the child commenced to vomit at intervals, and a fortnight after admission the temperature rose and continued to be irregular ( $99^{\circ}$ — $106^{\circ}$ ) until death four weeks later. On February 22nd nystagmus developed, which seemed to be rotatory in the left eye and lateral in the right eye. On March 7th a copious discharge of clear cerebro-spinal fluid began from each ear, and continued until the end. There was no rigidity of the neck throughout, and Kernig's sign was never obtained. Death took place from gradual exhaustion. The total duration of the illness was at least  $4\frac{1}{2}$  months, dating from the first noticeable enlargement of the head.

At the post-mortem examination the body was found to be extremely wasted; the head appeared large in comparison with the body; the anterior fontanelle was widely patent, and the sutures separated, but not widely. At the root of the right lung there was a small caseous focus, proved microscopically to be of tuberculous origin, and there were a few scattered grey tubercles near the base of the left lung. There was a caseous bronchial gland. No evidence of tuberculosis was found in any other part of the body. There was found to be a large excess of clear fluid in the cerebral ventricles, at the base of the brain, and in the spinal theca. There was some thickening of the arachnoid in the interpeduncular space, and about the superior verum of the cerebellum. There was no evidence

of thickening or matting of the membranes in the region of the roof of the fourth ventricle. No lymph and no tubercle was found either upon the brain or cord. The lateral ventricles were very greatly dilated, so that they occupied the greater part of each hemisphere; the third and fourth ventricles were also much dilated, but the iter did not seem much larger than is normal. The central canal of the cord was not dilated. The veins on the walls of the lateral ventricles were distended; the choroid plexus was not distended or thrombosed. There was no evidence of thrombosis in any cerebral sinus. Both petrous bones appeared healthy. The brain substance was soft, but presented no other abnormality.

## DISCUSSION.

Dr. J. WALTER CARE said that he welcomed any evidence tending to show, as he had previously maintained, that the posterior meningitis of infants was not an isolated condition, but merely a special form of acute cerebro-spinal meningitis. It was a fascinating view that several apparently different varieties of meningitis might have the same cause, a cause especially liable to attack children and to affect the base of the brain, but, when of a more virulent type, tending to attack also older persons, and to spread over the convexity of the brain. The identity of these forms of meningitis might be held to be established from the bacteriological evidence, the clinical characters, and the post-mortem appearances now described. It was clear that there was every possible intermediate condition between the slight and very chronic cases, which after a protracted course of months ended in recovery, and the most acute forms, which terminated fatally in a few days. A similar research might well be prosecuted in regard to pneumococcus meningitis. As to the causation of the hydrocephalus, he had almost abandoned his previously held view in favour of the mechanical theory of Sir Thomas Barlow and Dr. Lees, but it would appear that the last word had not been said on this point. There was much to be said in favour of the mechanical view in the protracted and more advanced cases; it seemed almost certain that in them there was obstruction, but not necessarily at the foramen of Magendie, possibly higher up—in the aqueduct of Sylvius, or lower down—in the upper part of the spinal canal. The composition of the fluid in the cases of chronic hydrocephalus following basic meningitis was also in favour of the obstruction theory, the absence of albumen and the low specific gravity not suggesting an inflammatory exudation. He referred to a recent case in which it seemed to him that dilatation must be due to chronic obstruction,—the case of a child with hydrocephalus following posterior basic meningitis, in whom he had tapped the lateral ventricles and drawn off normal cerebro-spinal fluid; and on subsequent tapplings fluid having quite the same characters was drawn off, thus negating an inflammatory origin. It was, however, a strong point against this theory that the intra-cranial pressure could be lowered by lumbar puncture, as seemed to be proved by some of Dr. Wall's cases. Kernig's sign he also had found not altogether reliable; in several proved cases of meningitis he had seen of late it had been absent throughout, and he had found it present, moreover, without any nervous disease whatever being discovered at the necropsy.

Dr. HERBERT FRENCH asked whether a diagnosis could be made by a simple microscopic examination of the fluid withdrawn by lumbar puncture, or whether it was necessary to cultivate the organism. He also asked if lumbar puncture was of service from the point of view of prognosis, whether it could be used as a means of treatment, whether it should be repeated, and if so, how often.

Dr. F. E. BATTEN alluded to the presence of blindness as one of the most characteristic features of the disease, and to the fact that in spite of the blindness the pupils reacted to light. He asked if Dr. Wall could give any explanation of the blindness, and an opinion as to the seat of the lesion; it was almost certainly not due to any affection of the lower path.

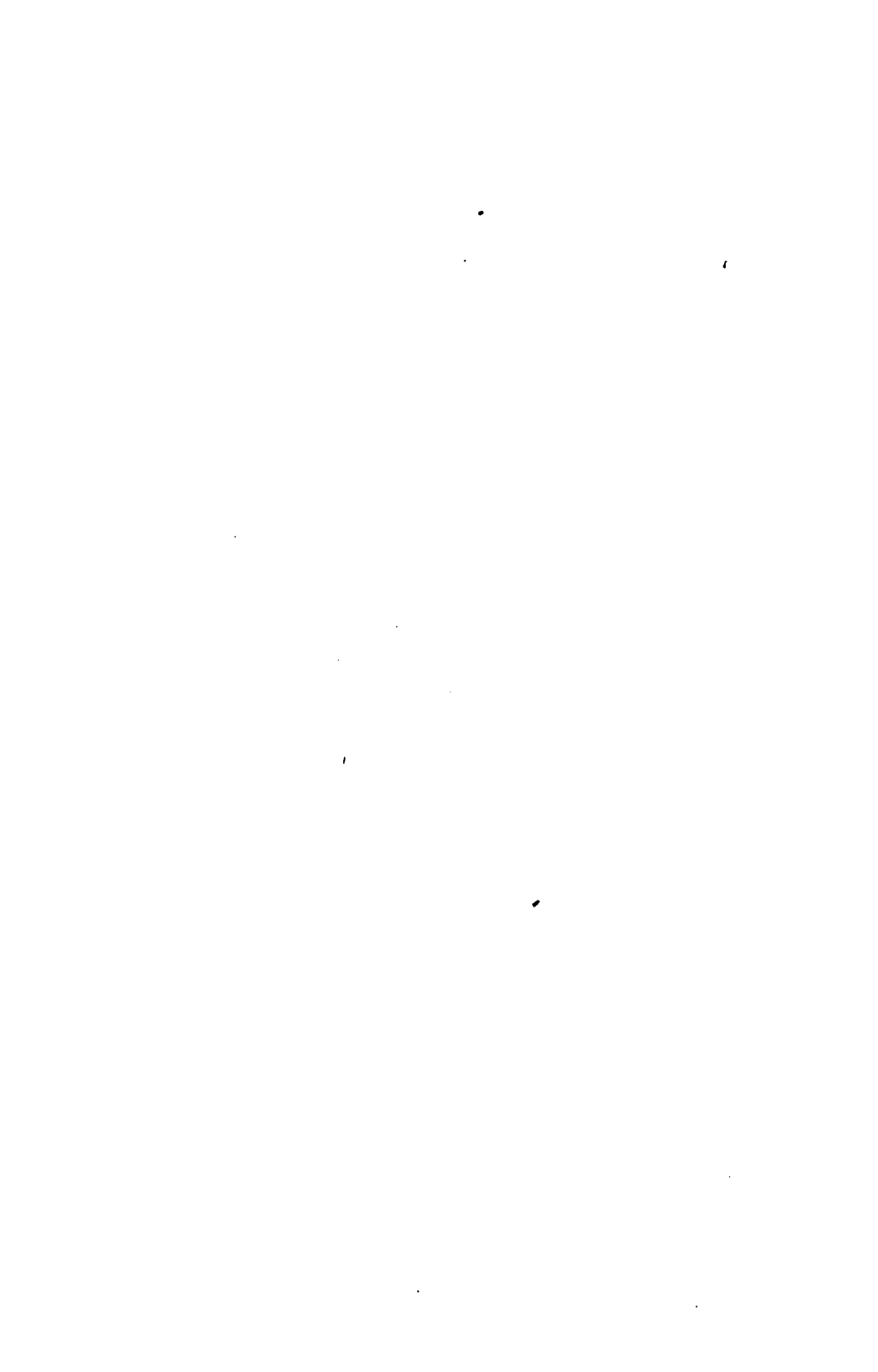
Dr. R. L. BOWLES remarked that the source of infection was doubtful. He referred to three cases of the disease which occurred in children of the same family, two of whom recovered completely, but the third never wholly recovered, and was always the subject of headache. The source of the illness had been attributed to the results of the decomposition of a brace of partridges which had by misadventure been concealed. Other cases of meningitis which he had believed to be tuberculous had recovered. Other cases were alluded to in which recovery occurred after the administration of mercury.

Dr. G. NEWTON PITT referred to the case of a boy, aged ten, suffering from chronic hydrocephalus, which was attributable to basal meningitis, in whom the central canal of the spinal cord was found at the necropsy to be dilated.

Dr. WALL, in reply, said he had not himself yet seen a case with dilatation of the central canal of the cord; such must certainly occur. The mechanical view, he thought, would ultimately have to be disposed of. He had seen several cases of chronic hydrocephalus, in which lumbar puncture had been followed by marked and immediate fall in the intra-cranial pressure. One case was referred to in which laminectomy was performed so as to establish permanent drainage of the cerebro-spinal fluid; the skull at once collapsed; the child was nursed with head downwards for several days, but the flow of fluid was so great that it died after a few days. After lumbar puncture had been performed, microscopical examination of the fluid was not by itself sufficient; complete bacteriological investigations were required; this was done in all the cases quoted. The usefulness of lumbar puncture from the point of view of treatment was, in the early stages, little or none, but in the later stages, with increased intra-cranial pressure, it relieved symptoms. In some cases it had been required to be repeated ten or fifteen times. The causation of the amaurosis, with retention of some of the lower forms of sensory perception, was possibly to be attributed to an encephalitis affecting the higher cortical centres. He could find



no antecedent causal conditions in his cases, and no evidence of contagion; the only thing was a possible lung affection as a source, but this was not by any means certain. Allusion was made to the after effects, and one case of imbecility was described. By Netter alone was evidence of contagion obtained, and by him the meningitis was held to be pneumococcal.



THE CLINICAL ASSOCIATIONS  
OF  
REDUPLICATED FIRST SOUND

BASED ON A SERIES OF ONE HUNDRED AND NINE CASES

BY  
ARTHUR G. PHEAR, M.D.

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It is no uncommon experience in the course of the routine examination of the heart to find that the ordinarily single first sound is replaced by a sound which is definitely double. Notwithstanding the large number of observers who have given their attention to reduplications of the first sound, opinions are still divided, both as to the cause of the phenomenon, and the clinical significance that attaches to it.<sup>1</sup> In the present communication, based on the study of a series of 109 cases which have come under the writer's notice, an attempt will be made to elucidate some of the matters in question.

<sup>1</sup> An admirable summary of the views held by different writers is to be found in the text-books on 'Diseases of the Heart,' by Byrom Bramwell and by Gibson.

Reduplication of the first sound is never perfect in the sense that there are two separate sounds divided by an appreciable interval of silence; it is more accurately described as an interruption in the uniformity of the sound by two points of emphasis. There is, in fact, continued sound with double accent. The two accentuated parts are alike in quality; as regards loudness they often differ, the accent falling more usually on the second than on the first of the two parts. In point of time they are heard in close succession, and both parts fall within the period of ventricular systole as timed by the impulse. The duplicate character of the sound is generally evident at the apex-beat, but not with such distinctness as at a point a short distance to the right, intermediate between the apex-beat and the sternal margin; it is seldom appreciable above the level of the fourth cartilage.

The phenomenon, first described by Bouillaud<sup>1</sup> in the year 1847 as the "bruit de galop," was probably an example of the reduplicated first sound. He noted the fall of the accent on the second part of the double sound, and since the rhythm thus produced resembles more or less closely that of a galloping horse, he gave to it the appropriate name of "bruit de galop," a term which has the merit of being descriptively accurate, while it involves no unproved theory as to the mechanical production of the double sound.

It is important to distinguish the "bruit de galop" with the rhythm of iambic verse,  $\cup - | \cup -$ , from the so-called "cantering rhythm," comparable to the dactyl,  $- \cup \cup | - \cup \cup$ . The term "cantering rhythm" should be reserved for instances of simulated reduplication of the second sound,<sup>2</sup> for the earliest recorded description

<sup>1</sup> Vide 'Clinique médicale de la Charité,' Potain, Paris, 1894, pp. 34 et seq.

<sup>2</sup> Vide a paper by the author on "Reduplication of the Second Sound," 'Lancet,' Jan. 9th, 1897; also a paper by Dr. T. Stacey Wilson on "Spurious Reduplication of the Second Sound at the Apex," 'Clinical Society's Transactions,' vol. xxxiv (1901), p. 10.

of which we are also indebted to Bouilland.<sup>1</sup> He gave to it the name "bruit de rappel," and compared its rhythm to "the noise of the hammer, which, after striking the iron, falls on the anvil, rebounds, and falls again motionless." The clinical significance of the "bruit de rappel" is entirely different from that of the "bruit de galop."

From an analysis of the cases on which this paper is based, it appears that the common clinical conditions with which a reduplicated first sound may be associated are as follows:

1. Valvular lesions of the heart, for the most part mitral regurgitation. There were eight examples of this, in all of which the mitral valve was incompetent.

2. Arterial degeneration, with raised systemic tension and accentuated aortic second sound. The reduplication of chronic interstitial nephritis, being always associated with cardio-vascular lesions, falls under this heading. There were thirty-two examples in all, of which four gave a definite history of strain, in eight there was evidence of lead-poisoning, and eleven were associated with renal trouble.

3. Pulmonary emphysema, with or without bronchitis (twenty cases).

4. Anæmia, chiefly of the chlorotic type, with the usual circulatory disturbances, including an accentuated and sometimes reduplicated pulmonary second sound (eleven cases, all in females, of ages varying from thirteen to twenty-six).

5. In cases whose prevailing symptoms are those of dyspepsia—discomfort after food, flatulence, constipation, and the like—there may be reduplication of the first sound without any other evidence of cardiac inefficiency; the present series includes thirty-one such cases, of whom twenty-six were women. There remain seven cases which do not fall into any of the preceding groups.

One or two points of interest arise from the analysis.

<sup>1</sup> 'Traité clinique des Maladies du Cœur,' second edition, 1841, vol. i, p. 218.

*Valvular lesions* other than mitral incompetence were rare. In three cases an aortic systolic murmur was heard as well as the mitral murmur; no cases were met of reduplication with established mitral stenosis or with aortic regurgitation. The second group, comprising cases of arterial degeneration with high tension, is remarkable for the large number in which the occupation involved contact with *lead*, with or without other manifestations of plumbism. The association is so frequent that reduplicated first sound must be regarded as one of the usual clinical signs of the cardio-vascular lesions caused by lead; indeed, I believe it is exceptional, on examining those who work with lead and whose arteries are thickened, *not* to find this modification of the first sound. The cases associated with *albuminuria* form only a small proportion (8.25 per cent.) of the total number in the series. Great importance has been attached by Potain and other French writers to the reduplicated first sound as an indication of chronic renal disease. The sign is undoubtedly present in many cases of granular kidney, but considering its frequent occurrence under other circumstances it would seem that its diagnostic value in this direction has been over-estimated.

Those who have inquired into the manner of production of the double first sound may be regarded as belonging to one or the other of two schools, according to the opinion they hold. On the one hand are the observers who maintain that there is no such thing as a true reduplication of the first sound in the sense in which the second sound may be reduplicated. They hold that the reduplication is not real, but simulated, an effect of doubling being produced by the interpolation of an abnormal sound immediately preceding the first sound proper. On the other hand are those who believe that the double effect does not depend on an interpolated sound, but is caused by the separation from one another of certain elements which under ordinary conditions are

blended to form the normal undivided first sound. According to this theory the first sound is doubled or divided in a manner comparable to doubling or division of the second sound, with, however, the important difference that, whereas there may be a complete separation of the second sound into its aortic and pulmonary elements, the division of the first sound always remains incomplete.

The upholders of the interpolation theory base their claim chiefly on the grounds (*a*) that the first element of the double sound does not precisely coincide with the commencement of ventricular systole as timed by the impulse, but immediately precedes it,—that it is, in fact, a presystolic sound, as, they say, can be established by a careful determination of the relation of the sound to the beginning of systole; (*b*) that an appreciable interval of silence separates the two parts of the sound; (*c*) that a difference in quality can be detected between the two component parts,—the first or presystolic part is short and thud-like, as though it were produced by a sudden shock, while the second or systolic part possesses the dull sustained character of the normal first sound; (*d*) that there may coincide with the first part of the sound a presystolic jogging, which leaves its record in the curve of a cardiographic tracing, and can sometimes be detected by the hand. In criticism of these points I would observe that the two parts of the double sound occur in such close proximity that it becomes highly difficult, if not impossible, to establish the argument that they occupy different phases of the cardiac cycle, or that they are separated by an interval of silence. The impression I have gained from careful auscultation has been that both parts of the double sound are coincident with the impulse, and that they appeal to the ear not as distinct sounds separated by silence, but as points of emphasis in the course of continued sound. In regard to quality, I believe that any difference there may be is one of intensity and not of timbre; the two parts are similar in character, but not of equal loudness, and the advantage

in loudness usually lies with the second part. The cardiographic evidence in favour of presystolic impulse does not seem to me convincing. In many cases of double sound the tracing shows no indication of double impulse. In some tracings recorded as illustrating the bruit de galop there is an obvious wave, but it occurs in the mid-diastole at a point so far in advance of the systolic wave that the corresponding abnormal sound could hardly have given rise to the semblance of a reduplicated first sound. I think it probable that these belong to a different category from the cases under consideration, in none of which was I able to satisfy myself of the presence of presystolic impulse. Some of the cases afford an interesting proof that both parts of the double sound are, in fact, systolic. A man aged forty-one had fibroid arteries, with high tension pulse, polyuria, and nocturnal frequency of micturition; the urine contained a trace of albumen. The period of systole was accurately indicated by a prolonged mitral regurgitant murmur, characteristically smooth and uniform in quality and pitch. The first sound was reduplicated, both parts being clearly audible through the systolic murmur. The first part of the double sound marked the commencement of the murmur; the second part closely followed the first. Here was an



Diagrammatic representation of the cardiac murmur and sounds audible at the apex in case quoted.

- a. Reduplicated first sound with systolic murmur.
- b. Second sound.

instance in which the murmur provided the means of accurately timing the reduplicated sound, and it was perfectly clear that both components of the double sound fell within the systole. In other cases of mitral regurgi-



tation with reduplicated first sound, it was equally clear that the two parts of the double sound were comprised within the limits of the systolic murmur.

Although our knowledge of the mechanism by which the first sound of the heart is produced is still far from exact, there are good grounds for the generally accepted belief that it is of complex origin, and that among the factors concerned in its production not the least important is vibration generated in the auriculo-ventricular valves, due to the state of tension into which these membranes are abruptly thrown in the course of the ventricular systole.

As a rule the mitral and tricuspid valves are thrown simultaneously into tension, and the resulting sound is single.

Suppose, however, some factor to come into play of a nature to mar the perfect synchronism which marks the normal incidence of tension, there will result a doubling or division of the first sound such as has been described. That the doubling is incomplete depends on the fact that elements other than valve tension enter into the composition of the first sound. One part of the reduplicated sound is, on this hypothesis, attributable to mitral valve tension, the other part to tricuspid valve tension, while the general continuity of sound is due to the non-valvular components to which the unmodified first sound probably owes its quality of duration.

The view of asynchronous valvular tension is supported by a study of the clinical circumstances under which the reduplicated sound arises. Placing the group of dyspeptic cases, which offer certain special difficulties, on one side, the clinical associations are all such as tend to modify the pressure, either in the pulmonary artery or aorta, which has to be overcome before the ventricle concerned can expel its contents. It is immaterial which side of the heart is involved in the changed conditions of tension. The essential factor is a disturbance of the relation which normally subsists between the intra-ventricular pressure on

the right and left sides respectively, and a corresponding dissociation of the mitral and tricuspid elements of the first sound.

On this theory the reduplication which may be heard in many healthy individuals if the breath be held at the conclusion of a forced expiration, or if the heart be examined after some sustained and severe physical effort, such as running or rowing in a race, becomes at once intelligible. Similarly, the reduplication of emphysema and mitral regurgitation can be traced to the rise of pulmonary tension, which is a common result of these lesions. The reduplication of anæmia without mitral regurgitation is probably attributable to impairment of the cardiac tone, with deficiency in driving power on the part of the left ventricle. There necessarily ensues an accumulation of blood behind any chamber whose propelling function is impaired, and thus in anæmia the tension becomes raised, at first in the left auricle, subsequently in the pulmonary vessels; and the pressure against which the right ventricle has to act is increased as surely, though not to the same degree, as in mitral regurgitation. Competence of the mitral valve is no barrier to the backward influence on the pulmonary circulation of impaired propulsion on the part of the left ventricle, though, as a matter of fact, in many cases of anæmia there is the additional element of mitral regurgitation, as is shown by the systolic apex-murmur. The reduplication of anæmia is no more enduring than are the other signs of disordered function. When, under appropriate treatment, the general health is improved and the cardiac tone restored, the area of impulse gradually contracts to its normal extent, the hæmic murmurs disappear, and the component parts of the first sound are once more blended.

The temporary doubling that may be heard in the late stages of typhoid fever, or during convalescence from this or other debilitating maladies, is probably

analogous in its production to the reduplication of anæmia.

There is one morbid condition in which, above all others, the normal relation of right to left intra-ventricular pressure is likely to be altered. In mitral stenosis the obstruction which deprives the left ventricle of its proper complement of blood is, at the same time, productive of pulmonary congestion, and leads to an increase of the resistance opposed to the right ventricle. Until the stage is reached at which relief is afforded to this ventricle by tricuspid regurgitation, the tension within its cavity during systole must be raised to a remarkable degree. Notwithstanding this, reduplication of the first sound is seldom, if ever, heard in cases of established mitral stenosis. It may sometimes be present in the early stages, before the appearance of the characteristic signs, but I have never known it to occur in conjunction with a presystolic or diastolic mitral murmur. I would offer the explanation that in the more advanced degrees of stenosis the diseased valve is thickened and deformed to such an extent that under no circumstances is it capable of giving rise to a tension sound. In this event the valvular components of the first sound, consisting wholly of vibrations produced by the sudden and excessive tension of the tricuspid valve, unmingled with vibrations generated at the mitral valve, cannot possibly be duplicate. The peculiarly sharp and abrupt quality of the first sound in mitral stenosis is intelligible on the view that it consists chiefly of an accentuated tricuspid sound, and that the stiffened mitral valve has no share in its production.

The clinical conditions so far described are such as tend to alter the relations between the two sides of the heart by an increase of the pressure against which the right ventricle has to act. A similar modification of the first sound may be effected by changes in the systemic blood-pressure. Instances are to be found in the reduplication that may arise in cases of arterio-sclerosis, due

to lead or other causes, chronic renal disease, and, as was first pointed out by Sibson,<sup>1</sup> acute nephritis. The last-mentioned observer threw light on the true nature of the reduplication in acute nephritis by an ingenious observation with the double stethoscope. Applying one of the two chest-pieces to the lower end of the sternum and the other to the apex, he found that, when both chest-pieces were in position, a double first sound was heard; when, on the other hand, either chest-piece was applied separately, the sound was single. He was thus able to establish that, of the two parts of the sound, the one was originated in connection with the right ventricle, the other in connection with the left.

If the hypothesis be correct that the double first sound is due to a lack of coincidence in the moments at which the mitral and tricuspid valves, being thrown into tension, give rise to sound, it is interesting to note that reduplications of the first and of the second sounds fall into line as regards the essential mechanism of their production. In both cases the doubling is attributable to asynchronous valve tension; there is, however, the difference that the second sound is purely one of valve tension, and it is accordingly possible for the aortic and pulmonary elements to be completely separated, with the result of perfect reduplication; whereas in the production of the first sound other factors besides valve tension are concerned, and the separation of the valvular factor into its two component parts, mitral and tricuspid, does not lead to a complete division or reduplication of the sound.

The view of asynchronous valve tension involves no hypothetical dissociation of one ventricle from the other in respect of muscular contraction; it is not inconsistent with a ventricular systole that from beginning to end is concurrent on the two sides. Nor does it imply a want of synchronism between the right and left sets of muscoli papillares; by the shortening of these muscles the valve

<sup>1</sup> "The Influence of Bright's Disease on the Heart and Arteries," F. Sibson, 'Lancet,' 1874, vol. i, pp. 437 and 505.

segments are doubtless drawn together, but it remains to be shown that their approximation exactly coincides with the moment at which the valve tension becomes such as to give rise to sound ; it would, indeed, seem on a *priori* grounds that the closure of the valves must be completed as a *preliminary* to the rapid rise of intra-ventricular pressure which is necessary for the production of sufficient tension to cause a valvular sound. What reduplication really signifies is a lengthening of the period between the closure of the valve and the production of sound on the side of the ventricle which has to meet the greater relative resistance.

It is sometimes assumed that the systole of the relatively burdened ventricle is prolonged, outlasting that of its fellow. This I do not believe to be commonly the case. If it were so, the closure of the semilunar valves on the affected side would be delayed, and the double first sound would be followed by a double second sound. As a matter of fact, combined reduplication of both sounds is uncommon ; with reduplicated first sound the second sound is usually accentuated, but not doubled, the accent falling on the pulmonary or aortic sound according to the associated conditions in regard to pulmonary and aortic tension. The increased resistance is probably overcome by an increased vigour of contraction on the part of the ventricle concerned, sufficient to compensate for the initial delay, and to bring the systole to a close at the same moment on the two sides.

It is sometimes stated that, as regards prognosis, a double first sound is an indication of undue stress and of impending cardiac failure. The statement is not borne out by the cases that have come to my notice, the greater number of whom were occupied with their usual work, and only attended hospital as out-patients. Cases have been under my observation for more than a year in whom the abnormal sound has persisted without change in its character and without any sign of cardiac failure.

## DISCUSSION

Dr. SEYMOUR TAYLOR classed cases with double first sound into those in which it occurred in diseased hearts and those in healthy hearts. A doubled first sound might co-exist with perfect health. In case of disease the double first was accompanied by a double second sound. The latter was heard better because it was more purely valvular, and free from the confusion of the muscle sound. In case of lead poisoning there was usually kidney disease and arterio-sclerosis leading to asynchronism of the two sides of the heart. The reduplication of the first sound was due to increased resistance in the pulmonary or systemic circulation.

Dr. ALEXANDER MORISON thought in discussing such conditions as heart-sounds it would be well to have a typical patient present, so that a clear idea of what was being discussed might be obtained. He had not found real reduplication of the first sound so often as described in the paper, or that it had been associated with serious cardiac lesions. A reduplicated first sound he considered to be a premature systole and a prolonged diastole, and he had observed it often follow change of posture. The causation of the first sound he associated with the concussion of the ventricular blood against the counter-pressure of the aortic blood.

Dr. PHEAR, in reply, thought there might be regurgitation through a defective valve, and yet the valve give rise to tension sounds that were independent of actual closure. Reduplicated first sound had not a very serious prognosis, but he had not had the opportunity of looking for it in presumably healthy persons, as was afforded, for example, in the course of examination for life assurance.

THE CLINICAL HISTORY AND SYMPTOMS OF  
ONE HUNDRED AND TWENTY CASES  
OF  
EXOPHTHALMIC GOITRE

BY

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(COMMUNICATED BY SIR THOMAS BARLOW, BART., M.D.)

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WHEN Sir Thomas Barlow, the late Secretary of the Royal Medical and Chirurgical Society, honoured me by an invitation to read a paper, it occurred to me that a short review of the main features in the clinical history and symptoms of the cases of exophthalmic goitre which I have seen during the last eleven and a half years, while in practice in the North of England, might be of interest to the Fellows of this Society. During this period I have taken notes on 120 cases, and these form the basis of this communication. I regret that in many cases the

records are very brief and omit many details; still the main features have generally been noted, and can be utilised in comparing the frequency of certain symptoms. Owing to the circumstances of consulting and hospital practice, I have not been able in the majority of the cases to make continuous observations like those recorded by Mr. A. Maude, of Westerham, as many of my cases have only been seen once or on a few occasions at longer or shorter intervals.

We may first consider the circumstances of the patients which may have any bearing upon the conditions under which the disease arises.

*Sex.*—Of the 120 cases, 110 were women and 10 were men, showing an exact proportion of 11 to 1. This emphasises the well-known fact that women are much more liable than men to suffer from Graves's disease. Of the 110 women, 57 were married, 1 was a widow, and 42 were single. Of the 10 men, 2 were married, 1 was a widower, and 3 were single. The social state of the remaining 10 women and 4 men was not recorded.

*Locality.*—In 86 cases the county in which the patient lived was noted. Forty-one lived in Northumberland, 37 in Durham, 3 in Yorkshire, and 1 each in Aberdeen, Buckingham, London, Rutland, and Stafford.

*Age.*—In considering the age of the cases I have taken the age at which the symptoms were first noticed, and not when the patient was seen. This was ascertained in 97 cases. The onset in some cases was insidious, and so the age at which the disease actually commenced could only be fixed approximately. In those cases in which there was a history of goitre long antecedent to the other symptoms, the age of onset taken was that at which other symptoms developed in addition to the goitre. The youngest case was fifteen and the oldest sixty-five at the time the disease developed. For convenience the cases have been arranged in quinquennial periods from fifteen to fifty-five which gives the following result in tabular form :



TABLE I.

Age.	Males.	Females.	Total.
Between 15 and 20 . . .	2 ...	14 ...	16
„ 20 and 25 . . .	2 ...	17 ...	19
„ 25 and 30 . . .	0 ...	16 ...	16
„ 30 and 35 . . .	4 ...	14 ...	18
„ 35 and 40 . . .	0 ...	4 ...	4
„ 40 and 45 . . .	0 ...	10 ...	10
„ 45 and 50 . . .	1 ...	7 ...	8
„ 50 and 55 . . .	0 ...	4 ...	4
Aged 58 . . .	0 ...	1 ...	1
„ 65 . . .	0 ...	1 ...	1
	<hr/> 9	<hr/> 88	<hr/> 97

Thus from fifteen to thirty-five nearly an equal number of cases started in each period of five years, and in these twenty years preceding the age of thirty-five 69 cases developed, as compared with 26 which commenced in the twenty years following that age. If we take the whole period of fifty years from fifteen to sixty-five we find that 69, or five sevenths of the cases developed in the first twenty years, as compared with 28, or two sevenths, in the remaining thirty years. These figures show that the greatest liability to the disease exists from fifteen to thirty-five years of age.

*Heredity.*—There was no history of exophthalmic goitre in either of the parents in any case. Two of the cases in the series were brother and sister. One female patient's sister had died of exophthalmic goitre. One case came to see me with two of her sisters, who are not included in the series, both of whom had had goitres as long as they could remember: one had also pigmentation of the skin, and the pulse was 108; the other, who was pregnant, had also a dark skin, and the pulse was 100. Another patient's sister had slight symptoms of goitre, tremors and nervousness, but the pulse was 86, and so she is not included in this series. In one case a paternal aunt had exophthalmic goitre, lived for twenty years afterwards, and ultimately died from diabetes; in another a maternal

aunt suffered from exophthalmic goitre. The father of one case had a goitre, while her sister had goitre, rapid pulse, and tremors. Two of the male cases had each a sister with simple goitre.

*Exciting cause.*—In some of the cases certain circumstances appeared to have a definite relationship to the onset of the disease, and may be considered as exciting causes. Sudden or prolonged grief and anxiety were the most important of these. Thus, in one case which I saw with Dr. Mearns, of Gateshead, a sister who also had severe exophthalmic goitre was found dead in bed nine months before the symptoms developed in our patient. In one case the sudden death of a brother, in another the sudden and unexpected death of the father in the presence of the patient one year before the goitre appeared, and in another the sudden death of the mother who suffered from "fits," appeared to be connected with the development of the disease. As examples of prolonged anxiety may be mentioned one case in which the prolonged illness and death of the patient's *fiancé* from phthisis were considered to be the cause of the illness; in another case a wife had nursed her husband up to his death from phthisis, and when I saw her was suffering from early phthisis as well as from exophthalmic goitre. In other cases overwork and mental anxiety had also played their part. Of acute illnesses, influenza in three cases, and scarlet fever in one case, had shortly preceded the onset of the symptoms. In one case sudden arrest of menstruation for seven months after a wetting during a menstrual period, and in another hard work in front of a hot furnace causing profuse perspiration, were supposed to be the exciting causes. In only two of the cases did an accident contribute to the development of the disease. In one of them a bundle of wet clothes fell from a height of some twenty feet on to the patient's head, and the symptoms appeared a month afterwards. In the other case the patient fell off a plank into deep water, and was nearly drowned; six months afterwards the goitre ap-

peared, eighteen months later palpitation, and seven years after the accident she had well-marked exophthalmic goitre; her sister, who was with her, went into the water after her; eight years later she also developed a goitre, followed by palpitation and tremors; as, however, her pulse was only 86 when I saw her she is not included in this series.

In some of these cases it may be objected that the interval is too long, and that it is merely a case of *post hoc* and not *propter hoc*. I have, however, thought it well to mention them, as the patients themselves attached considerable importance to the events just related.

*Onset.*—The onset was usually gradual, though in some cases it was more rapid. In one interesting case which I saw with Dr. Howard, of Buckingham, the disease started suddenly one night with violent palpitation and headache; by the end of a fortnight there was a well-marked enlargement of the thyroid gland and exophthalmos in addition to the rapid pulse. In another case palpitation and dyspnoea came on suddenly, and a week later there was enlargement of the right lobe of the thyroid gland and nervousness.

The first symptom most commonly noticed was the goitre. Thus, taking eighty-seven cases in which either one symptom or two symptoms simultaneously appeared before the others, an enlargement of the thyroid gland was the first sign of the disease in forty-three. This number, however, includes those cases in which a simple goitre preceded the other symptoms by a distinct interval, and which will be referred to again.

In nineteen palpitation was complained of before the other symptoms were noticed. In four only was the exophthalmos the first symptom, and in the same number either nervousness or tremors were first noticed. In one case rapid respiration was the first symptom which developed. Palpitation and nervousness or other nervous symptom developed at the same time in seven cases, exophthalmos and palpitation in four, goitre and palpitation

in three, exophthalmos and goitre in one, diarrhoea and excessive perspiration in one.

### SYMPTOMS.

*Thyroid gland.*—In considering the symptoms present in these cases we shall take the thyroid gland first. This was enlarged in 112 cases at the time the patient was examined. In 5 cases there was a history of previous enlargement, which had disappeared before the case was seen. In only 3 cases was there entire absence of enlargement both before and at the time of the examination. Thus goitre was present at some period of the attack in 117 cases, and entirely absent in only 3 of the 120 cases. These figures emphasise the fact that the enlargement of the thyroid gland is a very frequent symptom, which was only absent in  $2\frac{1}{2}$  per cent. of my cases. It not infrequently occurs that a patient who has had for some time a simple goitre with only local signs develops other symptoms of exophthalmic goitre at a later stage. In at least fourteen cases there had evidently been a simple goitre for some years before other symptoms were observed. In one case the goitre had been present 34 years and in another 32 before the onset of other signs of Graves's disease, and in other cases for varying periods of approximately 25, 18, 12, 10, 8, 6, and 3 years. Why this should occur in some cases of simple goitre and after such varying periods of duration is difficult to explain. Thus in June, 1899, I saw a brother aged nineteen and a sister aged sixteen; the former had a soft parenchymatous goitre of nine months' duration, and the circumference of the neck was seventeen inches; the latter had a similar goitre of six months' duration, the circumference of the neck being fourteen inches. Only local symptoms were present in both cases, the brother's pulse being 72 and the sister's 88. I saw the brother again in November, 1901, when he had well-marked Graves's disease, with a loss of some  $2\frac{1}{2}$  or 3 stones in weight, a pulse of 106, restlessness,

tremors, and slight exophthalmos. The circumference of the neck was fifteen inches, though this diminution was largely due to the marked emaciation. I could find no explanation of the development of the Graves's disease in the brother while the sister escaped. The practical lesson to be learned from this not uncommon sequence of events is that in all cases of simple goitre in which surgical treatment is contemplated it is important to make sure that no symptoms of Graves's disease are present, such as tachycardia, tremors, etc. All cases of Graves's disease bear operations badly, and in the presence of such symptoms any operative treatment for the relief of goitre is more dangerous, and is therefore, if possible, to be avoided, except in cases where some local condition, such as compression of the trachea, is so marked as to render an operation for the relief of the dyspnœa imperative.

The degree of enlargement of the thyroid gland has been recorded as "slight," when the enlargement could be distinctly felt, but was not always sufficient to attract the patient's attention, as "moderate" when it was easily seen and felt, and as "considerable" when it was very obvious and disfiguring. In twenty-seven cases the enlargement was slight, in thirty-six moderate, and in twenty considerable. In one, in which the goitre had been present for thirty-four years, it was enormous, the circumference of the neck being twenty-three inches. In twenty-eight cases the size was not defined in the notes, and in eight there was no enlargement at the time of the examination, though, as already stated, in five of these there had been a previous enlargement.

In eighty-nine cases there is a note as to the character of the enlargement of the gland. This was generally uniform, the right lobe often being larger than the left, as it is in the normal gland. In only two cases was the left lobe larger than the right. In two cases the right lobe alone was enlarged, and in one the right lobe and the isthmus. In four cases an adenoma or cystic adenoma of the isthmus was associated with general enlargement of

both lobes. In one case the left lobe only was enlarged, and also contained a small adenoma or cyst. In one case there was an adenoma in the right lobe, and in another in the left lobe. In one case there was an enormous fibrocystic goitre of long duration. A thrill over the enlarged gland was felt in only fourteen cases, in thirty it was noted as being absent, and in the remaining seventy-six no note on this point was made. In thirty-three cases a bruit was heard over the goitre. In twenty-three of these it was systolic in time. In seven there was a continuous venous murmur, which in three became much louder with each systole of the heart. In one other case a venous murmur was heard outside the lateral lobes at the base of the neck. In seventeen cases it was noted that no murmur was present, and in the remaining sixty-eight cases this point was not noted.

*Circulatory system.*—The frequency of the pulse was distinctly increased in all the cases. In those which were seen on two or more occasions it was found to vary considerably, and in these I have taken the greatest observed frequency in each case. The frequency was recorded in 118 cases; in the other two it was increased, but the actual pulse rate was not recorded.

TABLE II.

Pulse frequency.		Number of cases.	
Between	90 and 100	.	3
„	100 and 110	.	8
„	110 and 120	.	8
„	120 and 130	.	20
„	130 and 140	.	15
„	140 and 150	.	31
„	150 and 160	.	11
„	160 and 170	.	11
„	170 and 180	.	1
„	180 and 190	.	5
„	190 and 200	.	0
At	200	.	5

The frequency of the pulse thus varied from 90 up to 200. In no less than sixty-six, or more than half the cases, the pulse was between 120 and 150. In thirty-one of these, or more than one quarter of the cases, it was between 140 and 150. The high frequency of 200 was counted generally during a temporary attack of palpitation, and was not persistent. Great variation was sometimes observed in the same case within a short time. Thus in one case the pulse rate fell in a few minutes from 180 to 140; an ice-bag was then applied to the præcordium, and in a quarter of an hour the pulse had fallen to 112.

The pulse was usually regular, small, and compressible. Irregularity of rhythm was observed in only eight of the cases, and in one other the pulse was irregular in force, but not in time.

*Heart.*—Murmurs occurred rather frequently. A systolic murmur, heard most distinctly in the second left intercostal space close to the edge of the sternum over the pulmonary area, was present in seventeen cases. In some of these cases this murmur was loud and very rough, almost purring in character. In sixteen cases a systolic murmur was heard at the apex, and in eight a systolic murmur was heard both at the apex and over the pulmonary area as well. In one of the cases in which a systolic murmur was heard at the apex over the mitral area the first sound was so much accentuated as to be distinctly audible when the ear was held several inches away from the chest. In one case a systolic murmur was heard over the inner end of the third left intercostal space, and in only one was a presystolic murmur heard at the apex. In twenty-four cases no murmur was heard at all, and in the remainder no murmur was noted. In one case there were occasional attacks of syncope, and in another attacks of vaso-motor angina.

As is usual in Graves's disease, pulsation was felt over a larger area than normal in the region of the apex-beat. Taking the lowest and outermost point at which pulsation could be distinctly felt as the apex-beat, it was found in

nineteen cases to be in the fifth left intercostal space in the nipple line. In exactly the same number of cases it was outside the nipple line at distances varying from half an inch to two inches beyond it. In one case it was in the sixth space in the nipple line, in one in the sixth space one finger's breadth outside the nipple line. In two cases it was in the anterior axillary line. In eight cases the impulse was normal or internal to the left nipple line. In the remaining seventy cases no special note of the position of the apex-beat was made.

*Eye symptoms.*—Although exophthalmic goitre is the usual name of the disease, it is important to bear in mind that exophthalmos is often absent. This absence of the most noticeable symptom of all not infrequently has led to the disease being overlooked. In my series a note was made of the condition of the eyes in 114 cases. In seventy-nine cases there was exophthalmos, in three there had been prominence of the eyeballs at an earlier stage, which had subsided before I saw them. In no less than thirty-two cases, or more than one quarter, there was no exophthalmos at all.

Von Graefe's symptom, a delay in the natural fall of the upper eyelids when the eyes are directed downwards, was present in thirty-six out of ninety-one cases in which the presence or absence of this symptom was specially noted.

Retraction of the upper eyelids, commonly known as Stellwag's sign, was observed in forty-seven cases; in twenty-nine it was absent, and in the remaining forty-four no mention of it was made in the notes.

On examining how these symptoms were combined I find that in thirty-three cases the exophthalmos was present alone, in nine retraction of the upper lids with widening of the palpebral fissure as a consequence occurred alone, while Von Graefe's symptom was present alone in only one case. All three symptoms were present together in twenty-seven cases, in eight exophthalmos and Von Graefe's symptom occurred together without



Stellwag's sign, and in eleven exophthalmos and Stellwag's sign without Von Graefe's symptom.

*Nervous system.*—A fine regular tremor of the hands, which is best seen when the arms and hands are extended in front of the patient, is one of the most constant symptoms in exophthalmic goitre. This statement receives strong support from my cases. In 111 cases this tremor was present. In some of these it was very well marked, in others slight, and in some it was not observed on every occasion. In six of these cases it was noted as being present in the feet as well as in the hands. Probably it was present in the feet in other cases as well, as this was not looked for in all. The tremor was generally quite regular in rhythm; in one case it was rather irregular; and in five cases, in addition to the ordinary fine tremor of the extended hand, there were irregular jerky movements of larger amplitude.

In four cases no tremor at all was found, and in five there is no note on this point.

A peculiar mental condition of nervousness is a common symptom in exophthalmic goitre. Such patients are generally in a state of suppressed excitement, similar to that of a man just before a boat race, or on the eve of an examination. In seventy of my cases this condition was present, in three cases it was absent, in the remaining forty-seven no special note was made as to the mental state. In some cases the patient's temper was irritable. Some were very emotional and easily perturbed by trifling events, such as would not upset their equanimity in health. Thus one patient stated she became alarmed when her husband was late in returning from his work, and, when assisting at a confinement, was more nervous than the patient herself. In some cases restlessness was a marked feature; this was specially so in one of the men, who, while talking, was continuously changing his position, crossing and uncrossing his legs, placing first one arm and then the other over the back of his chair. He, like some of the other cases, was remarkably insensitive

to cold, and in the depth of winter felt quite warm while wearing the lightest of summer clothing and no overcoat out of doors.

One male case had melancholia with suicidal tendencies, and used to cry for several hours at a stretch, and in another case there had been suicidal tendencies for three months following the last confinement. No evidence of insanity was observed in any of the other cases. In only two cases were definite hallucinations described. Both these patients were perfectly sane. One, on waking, saw figures standing by her bed; she had also seen a cat on the bed and had heard a bell ringing; the other used to see figures at the foot of her bed at night, the faces being those of people who were dead, which appeared just as she last saw them. This symptom was not systematically inquired for, and may have been present in other cases as well, for Dr. Henry Head has pointed out that patients seldom complain of hallucinations unless specially asked about them under favourable circumstances.

One patient complained of nightmare. Insomnia was present in four cases. One of these patients stated she could not sleep for nervousness, and another used to lie awake till 4 or 5 a.m.

Headache was complained of in five cases, and was usually of a migrainous type. In one other case there were attacks of migraine, during which the goitre was enlarged and the eyes became more prominent.

Sudden attacks, in which many of the symptoms became greatly intensified for a few hours, occurred in some cases. In one such attack, during which I saw the patient, she complained of feeling "numb" all over. The face became flushed, and there was profuse general perspiration. The temperature was 101° F., and the pulse 200. There were general muscular tremors. After an ice-bag was applied to the præcordium the pulse fell to 156. The attack lasted about four hours.

Weakness of the legs was complained of by fifteen

patients. Five of them stated that the legs felt weak, as if they would give way while walking. Seven complained that the legs actually gave way, and five of these fell or were unable to walk at the time in consequence of this sudden loss of power. One patient who fell when she was out walking was unable to rise again without assistance.

Various other nervous symptoms were observed in single cases, which are not sufficiently important to mention in detail.

*Skin.*—The skin generally feels warm, and may be flushed at times. It is very frequently moist from an increase of insensible perspiration or from actual sweating. In some cases the skin is nearly always moist, and at times there are profuse sweats as well. In seventy-six of my cases there was unusual dampness of the skin, and in fifty-five of them there was sweating. More or less pigmentation of the skin was observed in twenty-two, or rather more than one sixth of the cases. The brown pigmentation was most marked on the exposed portions of the skin of the face, neck, and hands. In several cases it was especially marked on the eyelids and around or beneath the eyes. In one the outer edges of the areolæ and the front of the leg showed the pigmentation most markedly. In one case there was general diffuse pigmentation of face, neck, forearms, and hands, with darker freckle-like patches on the backs of the hands and forearms. In one case the patient used formerly to suffer greatly from chilblains, which disappeared when she developed exophthalmic goitre. As she improved, however, the chilblains began to return. Loss of hair was noted in ten cases. This generally occurred in the earlier or more acute stages of the disease. The hair generally grew again as the other symptoms subsided. In two of these cases the scalp became almost entirely bald, and in one this was accompanied by loss of eyebrows and eyelashes as well.

*Respiratory system.*—Increased frequency of respiration was observed in some cases, but did not as a rule give rise

to any discomfort. In one case, which I saw with Dr. Messer of Lemington, rapid respiration was the first symptom which attracted attention, and as it appeared just after an attack of influenza, it suggested the onset of an attack of pneumonia. The respiration was 40 and the pulse 75. Later on when I saw the case the respiration was 36 and the pulse 150. By that time the ordinary symptoms of exophthalmic goitre had developed. I may add that in this case the disease ran a short acute course, with uncontrollable vomiting, and terminated fatally. Two of the cases suffered from phthisis, and in another there had been some hæmoptysis, but there were no physical signs of pulmonary disease. In two cases there was expectoration of a large amount of watery mucus; in one of them about ten ounces of frothy clear mucus were expectorated each day for a week.

*Digestive system.*—Variations in the appetite were noticed in eleven cases; in four of these it was diminished, and in seven it was increased, or there was actual craving for food; in three others the appetite was good. An increase in the appetite, when present, usually occurred in the early stages of the disease. Thirst was complained of in four cases. Vomiting occurred in seven cases; in two of these it was severe and continued, and largely contributed to the fatal issue. The most frequent symptom was diarrhœa. This usually occurred in the form of short attacks of painless diarrhœa of one or several days' duration. These attacks often started suddenly and terminated in the same manner. This liability to diarrhœa was noted in thirty-five cases, or rather more than one fourth of the total number. Constipation was present in eight cases. In four cases there was increased frequency of defæcation. This symptom must be distinguished from diarrhœa, as it may be mistaken for it by the patient. The bowels act twice or thrice each day, but the motions are quite normal in character.

*Urine.*—The condition of the urine was, unfortunately, only noted in nineteen cases. In four of these a trace of

albumen was found, and sugar was found in three; in one of these there were 15 grains to the ounce of urine, and in another 40 grains.

*Generative system.*—In the 110 cases in women some irregularity in menstruation was noted in twenty-three cases. Amenorrhœa for periods of varying lengths, from five months to eight years, was present in ten cases. In several of these menstruation ceased for a time during the earlier and more acute stages of the disease, and returned again as improvement in the other symptoms took place. In four cases the loss was scanty, in two it was irregular, and in three it was both scanty and irregular. In two cases menstrual loss was excessive, but in one of these this was accounted for by the presence of retroflexion and retroversion of the uterus. In two cases menstruation occurred too frequently, and the loss was excessive as well.

*Nutrition.*—Wasting is a common symptom, and in some cases the loss of weight may amount to several stones. Some loss of flesh was noted in forty-five of my cases. The loss of weight was usually greatest when other symptoms were fully developed, and a regain of weight was one of the indications of general improvement. Thus one case at the height of the disease weighed only six stones, and when seen again, eight years later, she had gained 3 stones 11 lbs., while the other symptoms had subsided.

The male case, who was seen in June, 1899, with simple parenchymatous goitre, and again in November, 1901, with fully developed exophthalmic goitre, had lost from two and a half to three stones in the interval.

*Course.*—The course of exophthalmic goitre is generally slow and protracted, and runs so differently in different cases that it is difficult to follow, and prognosis is often uncertain. As examples of the disease running a short course I may mention two of my cases—one favourable and the other the reverse. In one case, that of a single woman aged 29, the symptoms first commenced in

December, 1900, and were well marked in February, 1901, when the pulse was 144. After this she rapidly improved, so that by the following September the pulse had fallen to 72, and she was practically well and able to undertake the work of a sister in a children's hospital, the whole attack having lasted only nine months.

In the other case, a married woman aged 52, the symptoms had all developed after an attack of influenza eleven weeks before I saw her, and were well marked and severe. She had uncontrollable vomiting, to which she succumbed shortly afterwards. In most of the cases, however, the disease ran a much more chronic course, extending to several years. In one case little or no change took place in the patient's condition during six years. As a rule, however, there was first a period of gradual development of the symptoms, extending over many weeks or even months; this was followed by another period, during which the symptoms were more or less stationary, lasting for several months or even years, after which, in a favourable case, the symptoms gradually improved.

Even in the most favourable cases a patient after an attack of exophthalmic goitre seldom returns quite to the normal condition she was in before in the way a patient recovers, for example, from an attack of enteric fever. In a considerable number there is a practical recovery, so that the patient feels well and complains of nothing, but a careful examination often shows that the pulse is still unduly frequent and excitable, or the thyroid gland remains slightly enlarged, or there is rather a staring expression or some general nervousness. Thus in one of my cases there had evidently been well-marked exophthalmic goitre, commencing twenty years before I saw her, and from which she considered she had recovered. The pulse was 92, the eyes were slightly prominent, and there was retraction of the upper eyelids, but the thyroid gland had returned to its normal size. Out of forty of my cases in which the patient was seen from time to time, or

information obtained as to the course of the disease, seven died, two remained stationary, and thirty-one progressed favourably. Of these thirty-one in which improvement took place, nine practically recovered, though two of them afterwards had partial relapses, eight were greatly improved, and fourteen improved to a certain extent.

In none of my cases was exophthalmic goitre followed by myxœdema. I have only had the opportunity of examining one case in which this interesting sequence occurred in a patient shown by Dr. Scott Jackson, of Alnwick, at a meeting of the North of England Branch of the British Medical Association.

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## APPENDIX.

*Treatment.*—The treatment of exophthalmic goitre is a large question, and the time at my disposal will not permit of a detailed account of the treatment adopted in all my cases. I shall, therefore, confine myself to a short account of the lines of treatment which have proved to be most successful.

No hard and fast lines can be laid down for the treatment of this disease. The symptoms vary so much in different cases that in each one the treatment has to be adapted to the special symptoms present and the social position of the patient.

In the first place comes the general hygienic treatment of the patient. If the symptoms are severe, absolute rest in bed for three or four weeks is essential. In cases in which the nervous symptoms are predominant, or when there has been rapid emaciation, rest in bed may be combined with isolation, liberal feeding, especially with milk, massage, and electricity; in other words, a course of what is often known as "Weir Mitchell treatment" is of great service.

In less severe cases, and in cases in which rest in bed has already been carried out, it is well to regulate the patient's mode of life as far as circumstances permit of it. At least twelve hours should be spent in bed, from 10 p.m. to 10 a.m., breakfast being taken in bed. In addition to this, in many cases the patient should lie down from 2 till 3 p.m. and from 6 till 7. A quiet life in the country or at the sea-side, as free as possible from excitement or effort, is most suitable. As much time as possible should be spent in the open air, partly reclining on a deck-chair, and partly in taking gentle walking exercise, which may be gradually increased from half a mile up to three or four miles a day, according to the progress made. As cases of exophthalmic goitre do not feel the cold easily, and are not liable to catch cold, they can spend much time out of doors nearly all the year round.

Electricity is most useful in many cases, but is not sufficiently employed, owing to the modes of application recommended being too elaborate. The faradic current may be employed easily and efficiently by a method which was first described to me by Sir Victor Horsley. Two flexible metal electrodes, about four inches long and two inches wide, covered with wash-leather, which are connected by a small strap and buckle on each side, are moistened and accurately applied to the neck. One electrode is placed in front over the thyroid gland, and the other over the back of the neck; the straps are then tightened so as to keep them in position. The electrodes are connected with the secondary coil of a small dry-cell faradic battery, and sufficient current is turned on to produce a distinct prickling sensation. The faradic current should be applied in this way for an hour each night and morning for several months. Not only do patients feel relieved for a time by each application of the current in this manner, but I have seen steady improvement take place under its continued use.

In many cases no special diet is necessary. When there is any emaciation a liberal diet is required, which may be



supplemented by two extra pints of milk in the day. If there is great emaciation forced feeding may be necessary.

In a large number of cases, and especially in those which are seen in hospital out-patient practice, we can unfortunately carry out little more than medicinal treatment, and often under circumstances which are not at all favourable to recovery.

Belladonna was frequently prescribed, and was useful in some cases, but I have often been disappointed in the results of its use. To be of service in exophthalmic goitre any line of treatment should be steadily maintained for some weeks or even months, and patients often dislike to continue taking belladonna in sufficient doses to produce physiological effects. Convallaria has proved useful in cases in which the frequency of the pulse has been very high, and is more effectual in lowering the pulse rate than other cardiac tonics. Bromides are useful in cases in which there are marked nervousness and tremors. Arsenic is useful in nearly all cases, and may be combined with other drugs with advantage. The best results are obtained by giving small doses of three or four minims of Fowler's solution three times a day for a month or two, or for the first three weeks of each month for five or six months.

Of the animal extracts thymus and supra-renal tablets have both been of service. Thyroid extract is harmful, as it often exaggerates the symptoms, and should not be given in exophthalmic goitre.

Special measures are frequently required for the treatment of urgent symptoms. The sudden attacks of diarrhoea were readily controlled by laudanum and dilute sulphuric acid. Severe attacks of palpitation with very rapid pulse yielded to the application of an ice-bag to the præcordial area. Persistent vomiting in acute cases is difficult to treat. On the whole rectal feeding and the administration of morphia, either subcutaneously or by the rectum, gave better results than other lines of treatment.

## DISCUSSION

Dr. HALE WHITE summarises the facts of a series of his own cases. In one the mother of a patient had had the disease. Rheumatic fever was not uncommonly associated with it, either in the personal or family history. In many there was an association with mental disease; in many there was polyuria, and in some of these a copper-reducing substance was found in the urine; in others it was absent. Polyuria was an early symptom. The polyuria associated with a copper-reducing substance might pass away. Wasting and anæmia were very striking. Pigmentation occurred in several; in one it was as dark as that of Addison's disease. In several the disease followed influenza. What was the state of Peyer's patches in fatal cases? They were often enlarged. What was the meaning of this, or its connection with the severe diarrhoea? The thymus was also frequently enlarged. Of twelve cases in hospital six were dead; they were "bad lives."

In his experience just as good results were obtained where no medicinal treatment was employed as in those treated with drugs. Belladonna was rarely, if ever, useful; neither were thymus or supra-renal tablets. The best treatment was probably hygienic with a quiet life.

Dr. W. EWART remarked on the uncertainty of prognosis and treatment in this disease. It was, however, in many instances amenable to treatment. It probably depended on a chronic intoxication in susceptible subjects, and associated with which were structural changes. The diarrhoea which was so frequently seen, although partly paralytic, was probably toxic or fermentative. The thyroid changes even were probably the result of a toxic influence. In many cases it had seemed to him that gastric dilatation co-existed; he had found it, in fact, in all his own cases. Of chief importance was thorough treatment on hygienic lines. Arsenic was of value. In one case recovery occurred while the patient was taking thyroid tablets. He also had noticed a close association of the disease with rheumatism.

Dr. H. D. ROLLESTON, in reference to fright and anxiety as alleged causes of the disease, mentions the increased frequency of the cases since the war, and described the case of a yeoman who had served in South Africa. Crises occurred in some cases, resembling, but different from, those of paroxysmal tachycardia. A case was referred to in which the pigmentation had led to a diagnosis of Addison's disease. Enlargement of the spleen was sometimes observed, and this was associated with enlargement of other collections of lymphoid tissue. Fatal cases were, in his

experience, rare, therefore he would have thought the prognosis was not very bad.

Mr. A. MAUDE thought the most important point in the paper was the number of cases in which there had been a pre-existent parenchymatous goitre. Numbers of such cases had been recorded in France. The influence of locality was a point on which information was wanted. The disease was very rare in India and the East generally. In Calcutta and Lahore it was almost unknown, although parenchymatous goitre was very common. The same thing obtained in China. In regard to heredity, he had seen a man with the disease whose mother and maternal aunt died from it. Of a family of three daughters, all of whom had parenchymatous goitre, two developed the exophthalmic form. Many cases seemed to crop up during the siege of Paris, corresponding to the access of cases since the late war. Tremor was perhaps the most important of the symptoms, after the triad of exophthalmos, goitre, and tachycardia, and next to this the mental symptoms. The pathological changes in the thyroid itself had not been much investigated. He also had noticed a paroxysmal irregularity in the force of the heart-beats. Eye symptoms were not of great value except by way of confirmation. In almost all cases he had found insomnia. In one case he had seen a spotted pigmentation, particularly of the eyelids. After watching cases of Graves's disease for twenty-five years he had seen but three deaths—from influenza, peritonitis, and septic endocarditis respectively. All three died at or about the age of thirty-five. He had never seen an absolute recovery. The cacodyle preparations were of no greater use than Fowler's solution. Thymus gland substance he had found of use in a few cases, mostly those with intestinal symptoms. Nauheim treatment he had tried, but had not found it of any special service.

Dr. HECTOR MACKENZIE had of late seen more cases in men than formerly, in the proportion of six men to forty-six women. Most of his cases had come from the southern counties, and especially Kent. He had had one case from India. In private practice cases were seen at a later age than in hospital, showing that the disease in poor persons at any rate meant a damaged life. He had not observed much evidence of heredity, but he had observed emotional disturbance as a precedent, also influenza and rheumatism in 6 per cent. In three of the male cases the occupation was that of a railway servant, pointing to the effect of strain as an exciting cause. Of fifty-two cases, goitre was absent in five, and in six it had existed for years before other symptoms appeared. In two of the cases cardiac pain was marked. Organic heart murmurs were rare. Exophthalmos was absent in only two. In one case it was the only symptom appearing during three years. Tremor was hardly ever absent; psychical changes were also characteristic. In two complete

mental break-down occurred. Delusions of suspicion were, as Dr. Savage had pointed out, characteristic. In three there was persistent headache. In one case shortness of breath was very marked. Abdominal disturbance was pronounced in all severe cases. Albuminuria was present in six cases, polyuria in several, and alimentary glycosuria was easily produced in any of these by giving an excess of glucose. Emaciation was severe, usually disappearing with improvement, and sometimes being replaced by actual fatness, or even solid œdema of the legs. Death occurred in six of fifty-two cases. Relapses in improved cases were common, but practical cure occurred in a fair proportion. Treatment was mainly hygienic, namely, rest in good air; especially important was living out of doors for the greater part of the twenty-four hours, and this was easy because the patients were particularly tolerant of cold. He had found belladonna, bromides, iodides, and arsenic of especial use, and in that order. Electricity was of little value in his experience, but massage had proved beneficial.

Dr. H. BATTY SHAW referred to a case in a man whose sister had goitre, probably of the exophthalmic type, and whose son had exophthalmic goitre. He asked if chyluria or albumosuria occurred in the disease or epilepsy.

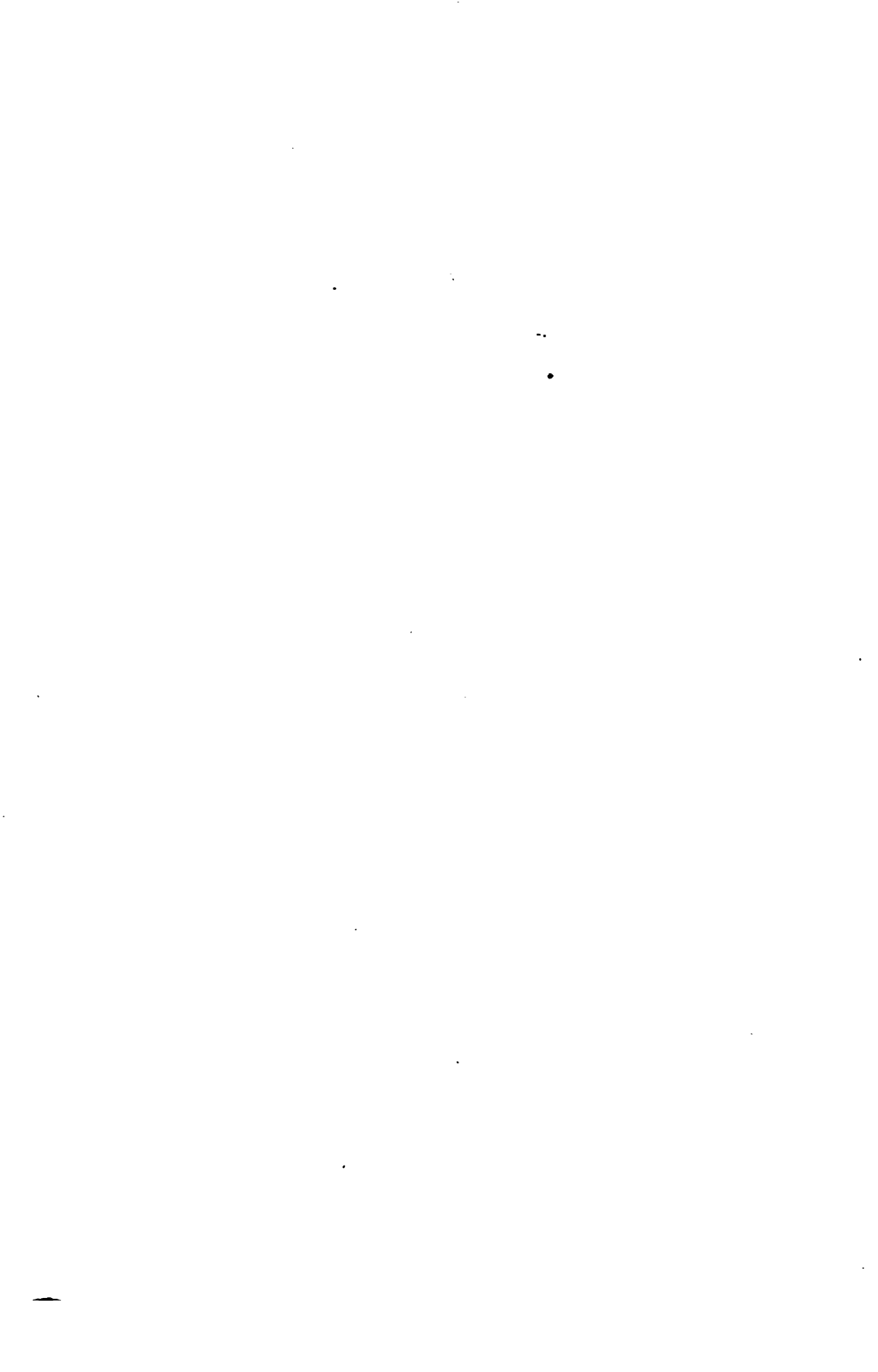
Dr. S. VEEB PEARSON mentioned that of 4000 deaths at St. George's Hospital during ten years only two were from this disease. In one of them, a female aged twenty, there was associated acute rheumatism and adherent pericardium. In the other, a female aged twenty-six, the thyroid was much enlarged, but it did not contain cysts; the thymus was persistent, and the left ventricle was hypertrophied and dilated.

Dr. W. BLAKE alluded to two cases in which improvement had occurred after giving thyroid gland substance; therefore he thought its administration could not always be harmful.

Dr. W. S. HERRINGHAM pointed out that in the paper the "forme fruste" cases were not included, namely, those in which goitre was absent, although the other symptoms were prominent. He had seen such cases admitted to the wards of hospital and later develop a goitre.

Dr. G. NEWTON PITT emphasised the point that often very severe cases obtained eventually a fair degree of health, and thought a too grave view was taken of the future of these cases. He had seen two very severe cases with marked emaciation make good recoveries. Even the worst cases, therefore, might pull round. He had not seen many cases completely recover—some exophthalmos usually persisted. Drug treatment was not, in his experience, of much value, yet it was of some. No drug was infallible. In two cases benefit had been obtained from supra-renal extract, but it had not been obtained in others; therefore in each case treatment should be tentative.

Dr. MURRAY, in reply, said he had found rheumatic fever, mental symptoms, and anæmia only very rarely in his cases. He had seen necropsies in three, but had not seen enlargement of Peyer's patches in any. The hospital patient was certainly a bad life. He had not detected gastric dilatation in any of his cases, although he was quite accustomed to finding it in patients, and had only once seen tachycardia continue alone; the other symptoms eventually developed. He had never seen exophthalmos alone, although he had seen a case which, recovering, showed this symptom after the others had disappeared. He had not met with albumosuria or epilepsy in his cases. He had seen thyroid substance do distinct harm in several cases. The disease seemed to be more common in the north than in the south of England.



# PAROXYSMAL HÆMOGLOBINURIA OF TRAUMATIC ORIGIN

BY

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THE following case of paroxysmal hæmoglobinuria is of unusual interest, owing to the dependence of the hæmo-  
globinuria upon self-inflicted injury.

The relationship between the hæmoglobinuric attacks and preceding or accompanying injury is so close and so constant as to preclude any other explanation than that the hæmoglobinuria is traumatic. No similar case appears to have been recorded; the one under consideration will therefore be described in some detail.

In the first section of this paper the patient's clinical history is given; in the second section the paroxysms will be described together with the accompanying changes in the blood and urine, so far as they have been investigated; and in the third section the relation of the paroxysms to self-inflicted injury is discussed, such references to the literature as have a bearing upon the condition being here given.

#### CLINICAL ACCOUNT.

The patient's father and paternal grandfather both died of phthisis, and his two brothers are both phthisical. His maternal grandfather was insane, and his maternal grandmother died from a stroke. His mother is at the present time an inmate of an asylum, suffering from delusional insanity.

As an infant the patient had frequent convulsions, and suffered from a chronic looseness of the bowels up to the age of fourteen, when he had an attack of pneumonia. He is stated to have been bright and intelligent as a child, going to school in the ordinary course. At the age of fifteen he went into service as a page, and from that time onward he gradually became dull and depressed, and soon unable to follow his employment. When sixteen years of age he had a "fit" of some kind, and took to his bed. He then began to suffer from attacks of dyspnœa, accompanied by much excitement, during which he beat himself about the forehead and thigh with great severity. This condition continued up to the time of his admission into the West Riding Asylum at the age of nineteen years.



The patient is now (*i. e.* at the age of twenty-four years) of average stature, but poorly nourished, and of slight muscular development. His circulation is very sluggish, there being generally some lividity and coldness of the hands and feet. His palatal arch is much contracted laterally, and there is also a slight degree of hypospadias. His general health is fair, and there are no definite signs of disease of the viscera. The patient exhibits dextrocardia.

The mental state of the patient has undergone no material change since his admission five years ago. He is suffering from dementia præcox.<sup>1</sup> His features and expression of countenance are coarse; he prefers to sit by himself, taking scarcely any interest in what is going on around him, and if questioned he either takes no notice or replies at random in monosyllables or short sentences, which he utters rapidly in an undertone. Nevertheless it is clear that he understands all that is said to him, for if told to do anything he always obeys, and occasionally observes objects quite intelligently. Left to himself he is restless and fidgety, occupying himself with trivial and purposeless acts, such as playing with his coat buttons or scratching on the wall, at the same time often smiling to himself in a vacant manner (Fig. 1) and talking rapidly in an undertone. He is an inveterate masturbator, is very untidy in dress, smears food or dirt over his clothing or his head, and is constantly dribbling saliva, with which his sleeves and the front of his waistcoat become saturated. He is attentive to the calls of nature. He exhibits no partiality for any of those around him, and is quite indifferent to his relations when they visit him. He has never, since admission, had any fits or shown any tendency to impulsiveness or maniacal attacks.

The patient has a habit of striking his forehead and the front of his right thigh with the palm of his right hand. Ordinarily the blows are not severe, and even

<sup>1</sup> As defined by Kraepelin, 'Einleitung in die psychiatrische Klinik,' 1901, Heidelberg.

when frequently repeated are incapable of producing any injury. Sometimes, however, the patient administers more vigorous blows, and at times he strikes himself, unless he is carefully restrained, with all the force of



FIG. 1.—Photograph of the patient. The extent and limits of the swelling on the forehead are shown. The thickened skin is soft and fairly movable over the frontal bone, both passively and when the patient contracts his brows. The colour of the skin is of a florid red or purplish tint, but no actual bruising is ever observable. Patient habitually smiles in a vacant manner, usually more so than the photograph exhibits.

which he is capable. The tendency to beating of the forehead and thigh is very variable at different times. For weeks the patient may merely administer one or several slight blows at occasional, and it may be rare intervals. At other times, without any obvious cause, the

patient's habit of striking himself undergoes an exacerbation, the blows being more frequent or more forcible, and not seldom the frequency and severity increase *pari passu*. Less often, and in association with the attacks of hæmoglobinuria which are about to be described, patient beats himself with extreme severity for a variable length of time, usually ranging from two or three to twenty minutes or even longer. These bouts, which will be further described in the next section of this memoir, can be prevented if the patient's hands are restrained for a sufficient length of time, the desire to strike himself passing off after a while, perhaps to reappear later. After a severe bout the patient may, as the list on pp. 184—188 shows, rest content for weeks or months with a few slight blows occasionally administered. On one occasion as many as nine bouts (Nos. 9 to 16) occurred in a single month, but this was a very exceptional number. Even when striking himself severely the patient acts in a mechanical manner, apparently paying little heed to what he is doing, and seeming quite calm and free from emotional excitement, though perhaps somewhat depressed. The patient cannot be induced to answer questions, so that we are not in possession of his own account of the attacks, and, as recovery is improbable, it is not likely that any introspective analysis of the bouts will ever be forthcoming.

The force with which the patient strikes his forehead is greater than that with which he strikes his thigh, and the former blows, in addition to being given at a greater mechanical advantage, are the more effective, owing to the thinner covering and larger extent of the frontal bone as compared with the femur.

It is not, therefore, surprising to find that the patient's forehead presents the swelling of the skin and subcutaneous tissue shown in Fig. 1. This swelling measures about four and a half inches transversely across and two and a half inches vertically. The increased thickness of the skin and subcutaneous tissue is not easy to

estimate, but, so far as can be judged, its thickness at no time reaches twice the normal. The skin in this situation is congested, and in cold weather is more or less livid, the congestion being marked after severe beating, and lessening considerably if the patient refrains for some weeks from striking himself with more than a slight degree of force. The same is true of the swelling, which, like the congestion, never completely disappears even after a period of prolonged rest.

The skin and subcutaneous tissue of the forehead where swollen is elastic, but in consequence of increased thickness, and to some extent also because of slight stiffening, it cannot be picked up in a fold. It is also less movable upon the frontal bone than is healthy skin. These alterations in flexibility and mobility are increased by marked beating, and diminished in the intervals.

The skin of the forehead does not exhibit any bruising even after severe beating. None of the various forms of discoloration following upon extravasation of the blood are met with, though the force used is at times such as would ordinarily cause bruising. This point will be again referred to in the third section of this paper.

No swelling or discoloration of the right thigh or palm is present.

## THE PAROXYSMS OF HÆMOGLOBINURIA.

### *Description of a Paroxysm.*

In order to give a clear idea of the paroxysms of hæmoglobinuria from which the patient whose case is under discussion suffered, it will be best to describe briefly the course of a single paroxysm, which may be taken as a type, and then to give in detail the condition of the blood and urine not only during the attacks, but also before and after, together with other facts in the patient's condition which are related to these.

On November 23rd some of the patient's urine was

passed in the ordinary course at 3 p.m.; it was of a clear yellow colour, and quite free from blood or albumin. There was at this time nothing unusual in the patient's condition; he was in his usual health, and there had been no definite change in his habits of life noticed during the morning or at midday. The patient, while under observation during the afternoon, was seated in a chair. At first he spent his time looking vacantly around and from time to time talking rapidly to himself in an undertone, as was his custom. At about 3.30 p.m. the patient began to pound his head and his right thigh above the knee (but especially the former) with the palm of his right hand, and to bite his clothes. He used extremely violent blows to his forehead, each blow being accompanied by a sickening thud. This continued for from twenty minutes to half an hour, after which the blows diminished in severity, and ceased entirely at about 4.30 p.m.

At 4.35 p.m. patient was induced to pass his urine (153 c.c.), which was lightly tinted of a bright red colour. At 5.40 p.m. he again passed his urine, this time only in small amount (26 c.c.), but of a deep florid red colour. At 7 p.m. the urine was again clear, was quite free from blood, and contained only a trace of proteid. There was thus observed in this, as in the other paroxysms, a bout of extreme violence shortly preceding the hæmoglobinuria.

Having thus described a typical attack of hæmoglobinuria, the state of the urine and blood must now be given more fully.

#### *Condition of Urine.*

*Hæmoglobin.*—The first specimen of urine passed during a paroxysm is of a more or less bright red colour with a slight admixture of brown, and this not unfrequently represents the whole attack. If a second specimen of urine containing hæmoglobin is passed the colour is more

distinctly brownish red, and is usually darker than the first. When a third specimen is passed the colour is much lighter, indicating that the paroxysm is nearly ended.

On spectroscopic examination of the urine in a thin layer (Fig. 2, B) only two bands between D and E, together with a fainter, broader band between b and F, are seen. Usually these bands alone are recognisable, but when a thicker layer is viewed (Fig. 2, A) a band between c and D

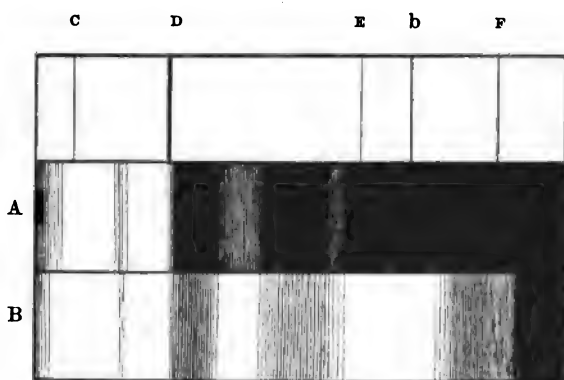


FIG. 2.—A. Spectrum of patient's urine (No. 7 in the list, pp. 183–186) containing hæmoglobin. In a layer two inches thick a faint band in the red was seen as in the diagram, almost the whole of the spectrum lying to the blue side of D being blocked out, only a faint light band being recognisable in the interval between the two oxyhæmoglobin bands, and a second, just recognisable, defining the larger oxyhæmoglobin band near E.

B. The same in a layer half an inch thick. Here it is difficult to recognise a band in the red, but the two oxyhæmoglobin bands can be seen, and also another band between b and F, as shown in the figure. The latter is due to the urobilin contained in the urine, and persists when all hæmoglobin has been precipitated by heat.

generally comes into sight, and if a very thick layer is examined this band becomes much more strongly marked, but the bands between D and E cannot be seen, the spectrum being cut off to the violet side of D. When the urine is boiled all the bands between C and E dis-

appear, but the band between b and f remains of little altered intensity, and is evidently the absorption band of urobilin, which, as already stated, is ordinarily found in the urine between the attacks.

The conclusion to be drawn from these observations is that the urine during the paroxysms contains principally oxyhæmoglobin, and that only a very small amount of another colouring matter, which we have not up to the present succeeded in identifying, giving an absorption band between c and d, and in this respect resembling methæmoglobin or acid hæmatin, is present. As is well known, in the acid methæmoglobin spectrum the band between c and d is always darker than any of the other bands, while in the patient's urine the absorption band in the red is, when present, always relatively very faint.

During a paroxysm of hæmoglobinuria the second sample of urine containing hæmoglobin is usually of a darker browner red colour than the first, so that further development in the urine of the pigment giving an absorption band in the red might be expected to occur on keeping, and in fact it was found that such did sometimes take place, though occasionally a diminution in the red band occurred. The same result was also obtained when the urine was kept, not at room temperature, but in an incubator at 37° C., the precipitate which, as is mentioned below, forms under these circumstances requiring to be filtered off before spectroscopic examination can be made. It may be suggested that acid hæmatin would be formed in the patient's bladder by the action of his acid urine upon hæmoglobin during a paroxysm. We have made many attempts to obtain a colouring matter presenting the spectrum of acid hæmatin by a prolonged action at 37° C. of the patient's normal urine upon dilute solutions of hæmoglobin, but invariably with negative results, though there is no difficulty in obtaining by the action of a 1 per cent. solution of acid phosphate of sodium upon hæmoglobin the spectrum of acid hæmatin. It may here

be observed that the patient's urine during all the paroxysms observed was acid when passed.

On keeping patient's urine in an incubator, even at so low a temperature as 30° C., a chocolate precipitate occurs at the end of from two and a half to six hours, resembling in appearance that present in the urine after standing, at the temperature of the room, for from twelve to twenty-four hours, and when this precipitate is filtered off the urine is still of a red colour, though somewhat weakened. When fractional precipitation of proteid in patient's urine was attempted, it was found that precipitation commenced at a temperature of 57° C., the first precipitate being finely flocculent in character and of a chocolate-brown colour. On raising the temperature to 62° C. a coarser precipitate of the same colour occurred, though precipitation was not complete until the urine had been kept for ten minutes at 65° C.

The amount of hæmoglobin present in the urine was determined in the following way:—A solution of the patient's blood, the hæmoglobin of which was laked, was prepared, having usually a strength of .5 per cent. of blood. In order that the estimation might be more accurately carried out this solution was made to contain 50 per cent. or more of the patient's normal urine. The urine passed during a paroxysm, which was darker than this solution, was then diluted until the tint of the two fluids was the same, the comparison being made in tubes of equal calibre held against a white background in daylight.<sup>1</sup> This method of estimation was generally easily carried out in the case of the first sample of urine passed, but in the case of the second the matching was not so perfect, owing to the distinctly browner tint of the urine.

The following are the amounts passed in six successive attacks. In each case the hæmoglobin is measured not as such, but in terms of the equivalent amount of

<sup>1</sup> A rough estimate could, it was found, be made more quickly by the use of Von Fleischl's hæmoglobinometer.



patient's blood, this latter being a convenient mode of expression.

TABLE I.

*Indicating the Amount of Hæmoglobin lost during the Paroxysms.*

Number of paroxysm.	Total hæmoglobin-content of urine during paroxysm in terms of patient's blood.	
6	...	2·97 grammes.
7	...	1·3    "
8	...	1·2    "
9	...	3·6    "
10	...	2·4    "
11	...	3·0    "

The amount of time which elapses between the commencement of the self-inflicted violence and the last appearance of hæmoglobin in the urine cannot be determined with certainty because, on the one hand, of occasional pauses in the beating of the forehead; and because, on the other hand, patient may retain his urine in the bladder for some time after the elimination of hæmoglobin has come to an end. It is, however, possible to fix a maximum for this period; thus, on reference to paroxysms 9 to 16 in the list given on pp. 019—022, it will be seen that the times elapsing between the commencement of the beating and the last passage of red urine were respectively 4 hours, 3 hours, 4 hours, 2½ hours, 5½ hours, 12 hours, 1½ hours, and 4½ hours, or an average of 4½ hours. It is interesting to note, as paroxysm 15 shows, that extravasation of blood, hæmolytic, and elimination of hæmoglobin in the urine may be completed within 1½ hours, though ordinarily the process is more prolonged.

*Other proteids.*—It would appear, from the fact that the precipitate caused by heat after the addition of acetic acid is always of the same chocolate-brown colour when fractional precipitation is attempted (p. 010) between the temperatures of 57° C. and 65° C., that the chief proteid

in the urine is hæmoglobin. Serum albumen and serum globulin do not make their appearance in the urine in recognisable amount, as is indeed to be expected. The urine between the attacks contains a small amount of nucleo-proteid, which is no doubt present also in the urine containing hæmoglobin, although this is not easily recognisable.

The remaining characters of the urine in respect of the paroxysms may be briefly referred to, being essentially negative, or not bearing any defined relation to the attacks. A considerable time was spent in the early part of this research, before the relationship of the paroxysms to external violence had been determined, in attempting to trace out some connection between the condition of the urine and the attacks. Thus it was thought that some variation in the condition of the patient's urine might precede or accompany the appearance of hæmoglobinuria indicative of some variation in the patient's general state, or that in addition to the appearance of hæmoglobin other variations might make their appearance. No such definite connection between the amount and composition of the urine and the paroxysms could, however, be traced, and indeed the variations ordinarily met with were so great as to preclude other than extremely marked changes being recognised. For this reason we omit most of this work, but Table II, selected from a large number of such observations, may be taken as a sample. It illustrates the condition of the urine during a paroxysm, and for five days before and after. A few points in the condition of the urine, which this table serves to illustrate, may be briefly mentioned.

*Amount.*—The amount of urine shows considerable variation, the lowest amount passed in twenty-four hours being 840 c.c., and the highest 2940 c.c. During the eleven days recorded in Table II the diurnal variations were much less; no constant alteration in the quantity was found to occur in connection with the paroxysms.

TABLE II.—*Showing the Condition of the Urine during a Paroxysm of Hæmoglobinuria and on the five days preceding and following the same.*

Date.	Amount in 24 hours.	Specific gravity.	Colour.	Deposit.	Total proteid.	Reaction.	Urea in grammes.
Nov. 2	1540 c.c.	1011	Amber	Nil	Nil	Acid	16.9
" 3	2072 c.c.	1020	Amber	Nil	Nil	Acid	22.1
" 4	1680 c.c.	1020	Amber	Nil	Nil	Acid	20.1
" 5	1792 c.c.	1015	Amber	Nil	Nil	Acid	17.9
" 6	1400 c.c.	1016	Amber	Nil	Faint trace	Acid	17.0
" 7, before 11 a.m.	1680 c.c.	1020	Amber	Nil	Trace	Acid	16.8
" at 11 a.m.	60 c.c.	1020	Amber	Nil	.06	Acid	1.1
" at 1.15 p.m.	60 c.c.	1030	Dark red	Nil	1.3	Acid	1.2
" at 3.40 p.m.	45 c.c.	—	Less dark red	Nil	1.03	Acid	.9
" 8	1790 c.c.	1016	Amber	Nil	.04	Acid	28.4
" 9	1400 c.c.	1020	Amber	Nil	Faint trace	Acid	15.4
" 10	1960 c.c.	1016	Amber	Nil	Trace	Acid	19.6
" 11	1540 c.c.	1012	Amber	Nil	Trace	Acid	13.8
" 12	1820 c.c.	1025	Amber	Nil	Faint trace	Acid	43.6

*Specific gravity.*—The specific gravity of the urine varies from 1·011 to 1·037, the higher figures being associated with the paroxysms when the specific gravity is usually above 1·020, although in a few samples it was 1·015 or lower.

*Reaction.*—This was invariably acid, both during the paroxysms and in the intervals.

*Urea.*—The amount of urea varies considerably, but is usually below that stated to be the normal diurnal quantity. Between the paroxysms it ranged usually between 14 and 27 grammes per diem. The urine containing hæmoglobin varies very much in its percentage of urea; thus the percentages of urea in six different samples of coloured urine was 2·0, 2·4, 1·2, ·2, 1·3, and ·6 respectively.

*Glucose.*—The patient's urine is always free from glucose.

*Other colouring matters.*—Of colouring matters other than hæmoglobin, urobilin is constantly present, giving a faint band between b and F. Indican is not present in more than traces in the urine.

*Deposit.*—The patient's urine is ordinarily free from deposit. Occasionally crystals of phosphates, urates, and oxalates are met with, and sometimes epithelial cells. Nucleo-albumin is frequently present in the urine in very small amount in the interparoxysmal periods. When the urine contains hæmoglobin it is generally quite clear when passed, but upon standing the chocolate-coloured deposit already referred to (page 010) is observed.

### *Condition of Blood.*

In order to determine if any change in the blood occurred in connection with the paroxysms of hæmoglobinuria numerous observations were made, directed to the number and aspect of the red cells, the percentage of hæmoglobin, the condition of the blood in respect of platelets, the number and relative number of the white cells, and the appearance of the plasma. These observations

TABLE III.—*Showing the Condition of the Blood during a Paroxysm and on the five days preceding and following the same.*

Date.	Red cells per c.mm.	White cells per c.mm.	Platelets per c.mm.	Finely granular per cent.	Eosinophile per cent.	Large hyaline per cent.	Small hyaline per cent.	Percentage of hæmoglobin.	Red cell index.	Proportion of white to red.
Nov. 2 . . .	3,880,000	5330	256,000	81	·8	5·0	13	72	·9	1 : 727
„ 3 . . .	3,800,000	7100	234,000	69	·6	10·6	20	72	·95	1 : 534
„ 4 . . .	3,200,000	4980	286,000	—	—	—	—	75	1·1	1 : 680
„ 5 . . .	3,186,000	5330	220,000	71	1·0	9·0	19	75	1·18	1 : 500
„ 6 . . .	3,189,000	4980	273,000	69	·6	10·0	21	75	1·1	1 : 640
„ 7, 1.30 p.m. 4 p.m.	3,870,000 4,128,000	6400 6750	231,000 294,000	73 69	·4 1·4	7·4 10·6	19 18	77 77	1·1 ·9	1 : 526 1 : 610
„ 8 . . .	3,488,000	4970	286,000	69·6	·2	10·0	20	75	1·07	1 : 700
„ 9 . . .	4,032,000	3550	224,000	66·6	1·0	10·2	22	75	·93	1 : 1100
„ 10 . . .	4,032,000	5330	256,000	72	1·2	7·6	19	77	·95	1 : 750
„ 11 . . .	4,088,000	5330	234,000	74	·4	8·6	17	77	·9	1 : 765
„ 12 . . .	3,914,000	4940	203,000	74	·2	8·4	17·4	78	·9	1 : 808

were made before, during, and after the hæmoglobinuric attacks, and owing to the irregular occurrence of the latter it was necessary to make an extended series of consecutive daily observations. Table III affords a good illustration of the variations met with.

*Red corpuscles.*—The number of red cells per c.mm. exhibited diurnal variations, ranging usually between 3,500,000 and 5,000,000. In Table III they range between 3,136,000 and 4,128,000, and exhibit a rise at the time of the paroxysm. This rise, however, was not present in many of the other paroxysms, and there is no constant variation in the number of red cells in association with the hæmoglobinuric attacks. In respect of form the red cells were regular at all times, they showed the usual tendency to adhere in rouleaux, and were free from any marked degree of variation in size or form.

*Percentage of hæmoglobin.*—The percentage of hæmoglobin in the patient's blood, estimated by von Fleischl's hæmoglobinometer, ranged usually between 70 per cent. and 80 per cent. No constant variation occurred in connection with the paroxysms.

*Red cell index.*—The patient's red cell index generally corresponded very closely to unity. The hæmoglobin content of the red blood-corpuscles was sometimes as low as .8, and sometimes reached 1.2. No definite alteration of the red cell index has been noted in association with the hæmoglobinuric attacks.

*Platelets.*—The blood-platelets were estimated with a Thoma-Zeiss hæmatocytometer, Hayem's solution being used as a diluent. The numbers obtained, which are only approximate owing to the inherent difficulty of estimation, varied between 75,000 and 300,000. There was, however, no marked increase<sup>1</sup> at any time in connection with the paroxysms. Sometimes a decrease occurred during the attack, and on one occasion, when four observations were made in the course of two and a

<sup>1</sup> Cf. Fraser, quoted by R. C. Cabot, 'The Clinical Examination of the Blood,' London, 1899.

half hours, considerable variation in the number of platelets counted was met with, the numbers observed being respectively 85,400 at 4.35 p.m., 135,100 at 5.10 p.m., 234,000 at 5.40 p.m., and 85,400 at 7.5 p.m. (beating of forehead from 3.30 p.m. to 4.30 p.m., red urine passed at 4.35 p.m. and at 5.40 p.m.: the attack is described on page 007).

*White cells.*—The number of white cells in the patient's blood varied at different times between 3500 and 7000, the average number being about 5000. The varieties of white cells are given in Table II, in connection with the paroxysm there described. The finely granular varied between 66 per cent. and 81 per cent., the mean being 72 per cent. The small lymphocytes were always more abundant than the large hyaline cells, the two together averaging 27.5 per cent., and the eosinophiles being rather more than .5 per cent. It was necessarily difficult to make many differential counts of white cells during the paroxysms owing to the uncertainty of their occurrence and the difficulty of ascertaining at the time whether the elimination of hæmoglobin was continuing or not, but the observations made so far do not reveal any alteration in the relative number of the different varieties of white cells in connection with the hæmoglobinuria.

*Proportion of white cells to red.*—The proportion of white cells to red varied generally within the limits of 1 to 500 and 1 to 800. No constant variation in this ratio could be discovered in relation to the paroxysms.

*Serum.*—The colour of the serum in a layer 1.5 mm. thick was a pale yellowish brown. When the clot was mechanically injured in removing it from the serum some of the red cells parted with their hæmoglobin, and the serum then gave a very faint oxyhæmoglobin spectrum. This, however, occurred in serum obtained during the interparoxysmal period as well as during the paroxysms, and was not more marked in the latter than in the former. We were not able to obtain evidence that the blood-plasma was tinted with hæmoglobin during the paroxysms, but

our observations on this point were not as complete as could be desired.

*Rate of coagulation.*—Coagulation of patient's blood in tubes varying in internal diameter from .5 mm. to 2 mm. took place at the end of three to five minutes, both during and between the paroxysms.

*Hæmolysis.*—Portions of patient's blood withdrawn in a capillary tube exhibited no hæmolysis on keeping for twenty-four hours, whether the blood was withdrawn during a paroxysm or not. Portions of the patient's serum added to a suspension of patient's red cells in physiological saline solution, to the extent of 1 per cent. of each, also failed to produce hæmolysis at the end of twenty-four hours.

Summing up what precedes, it may be stated, as the result of numerous observations, that all attempts to discover definite changes in the blood, standing in relation to the appearance of hæmoglobinuria, have so far been unsuccessful. The study of the condition of the patient's blood has involved a large amount of work extending over more than two years, and was originally undertaken under the impression that the cause of the hæmoglobinuric attacks was to be found in antecedent changes in the blood.

#### *General Condition of Patient.*

There was no recognisable alteration in the patient's general physical state before, during, or after the paroxysms, no affection of appetite accompanied the hæmoglobinuric attacks, nor was any change in patient's manner or habits or any variation in his temperature discoverable, so that these attacks cannot be regarded as febrile; the pulse and respiration rate were not altered to any noticeable extent.

It is an interesting circumstance that no enlargement of patient's spleen could be recognised in connection with the paroxysms.<sup>1</sup>

<sup>1</sup> Cf. Ponfick, 'Verhandl. des X Congresses f. innere Medicin,' 1891.



MODE OF PRODUCTION OF THE PAROXYSMS OF  
HÆMOGLOBINURIA.

In the preceding section a typical attack of hæmoglobinuria has been described. In the present section the course of events preceding and leading up to the passage of red urine will be considered at greater length, in order that the nature of the attacks may be more clearly defined.

The one obtrusive circumstance in connection with the paroxysms is the association with them of self-inflicted violence in the form of beating of the forehead. The constancy with which this in a severe form has preceded the hæmoglobinuria is well exhibited in the following list of some eighteen attacks, from which the patient suffered during a period of eight months.

*List of Successive Paroxysms occurring from April to  
December, 1901.*

No. 1, April 19th.—On the previous day patient was violent to himself, and on the day of the paroxysm of hæmoglobinuria pounded his forehead with exceptional violence.

Total proteid in urine, by Esbach's method, 1·2 grammes.

No. 2, April 25th.—Patient had a paroxysm associated with self-inflicted violence.

Total proteid in urine, by Esbach's method, ·15 gramme.

No. 3, May 10th.—Patient beat his head violently for three hours preceding the passage of red urine.

Total proteid in urine, by Esbach's method, ·16 gramme.

No. 4, May 27th.—Beat his head very violently for one hour and a half before passing a single specimen of porter-coloured urine (in previous attacks the urine was

much more red in colour). Quiet before and after the bout of violence.

Total proteid in urine, by Esbach's method, '36 gramme.

No. 5, June 9th.—Patient, who previously had been quiet, passed clear yellow urine, then beat his head violently for one hour. Three hours later passed red urine. During next four hours some beating of forehead, then passed another sample of red urine; quiet afterwards. Urine now of a clear amber colour.

No. 6, August 10th.—Urine passed at 3.30 p.m. amber in colour. At 5.30 p.m. passed 83 c.c. dark red urine, containing an amount of hæmoglobin equal to that in 2.49 c.c. of patient's blood. At 7.15 p.m. passed 5.7 c.c. containing hæmoglobin, the equivalent of .48 c.c. patient's blood. Urine amber-coloured at 11 p.m. and afterwards. It was reported of patient that he "never was so excited before." The violence lasted from 3.30 p.m. to 4.15 p.m. Patient struck his forehead occasionally subsequently.

No. 7, October 22nd.—Patient commenced to be excited about 10.30 p.m. on October 21st; beat his head very severely between 1 a.m. and 2 a.m. (The attendant stated that he had never seen patient so violent before.) He then gradually quieted down. Urine at midnight clear yellow; red urine at 3.15 a.m.; at 5 a.m. a smaller amount of darker red urine; amber-coloured subsequently.

Total amount of hæmoglobin lost was found to be equivalent to that contained in 1.3 grammes patient's blood.

No. 8, October 31st.—Patient was quiet up to 10.30 p.m. on October 30th, when he passed clear yellow urine. Shortly before 11 p.m. began to be excited, and from thence onward to midnight became gradually more and more violent, pounding his forehead with both palms, and biting his shirt. Patient's violence, though slightly less than in preceding attack, was nevertheless extreme

in degree. After midnight patient became quiet again. Urine passed at 12.5 a.m. light red in colour; that passed at 2.20 a.m. was brownish red; urine passed subsequently was quite free from hæmoglobin. Amount of hæmoglobin lost was equivalent to 1.2 grammes of patient's blood.

No. 9, November 3rd.—Patient began to be excited about 5 a.m., and then passed clear urine at 5.30 a.m. Was extremely excited, beating himself very severely for rather more than an hour. At 6.15 a.m. passed red urine, was quiet after; at 9.5 a.m. passed dark port wine-coloured urine; at 10.15 a.m. passed darkish amber-coloured urine. Amount of hæmoglobin lost was equivalent to 3.6 grammes of patient's blood.

No. 10, November 5th.—Patient beat his head very severely from 5.15 a.m. to about 6.30 a.m., after which he quieted down. Urine passed up to 6.30 a.m. was clear amber in colour; at 6.30 a.m. it was red in colour; at 8.10 a.m. dark brownish red; at 10.30 a.m. and subsequently amber-coloured.

Total hæmoglobin lost was equivalent to 2.4 grammes patient's blood.

No. 11, November 11th.—About 10.45 p.m. on November 10th patient began to be excited in the usual way. The beating of the forehead increased gradually, reaching a maximum about 12.15 a.m. At 12.30 a.m. passed clear amber urine. Patient then quieted down and went to sleep. At 2.45 a.m. awoke and passed red urine; at 4.5 a.m. passed clear amber-coloured urine.

Hæmoglobin lost was equivalent to 3 grammes patient's blood.

No. 12, November 13th.—Was excited, beating his head severely from about 8 p.m. to 9.30 p.m., when the violence became less severe, ceasing after 10.30 p.m. Urine passed at 9.30 p.m. amber-coloured; at 10.30 p.m. red; at 12.30 a.m. amber-coloured.

No. 13, November 15th.—Excited from 8 p.m. to about 10.30 p.m. There was severe beating of the head up to

10.30 p.m., but none after. Passed red urine at 10.30 p.m., and again at 1.30 a.m.; passed clear amber urine at 6 a.m.

Between November 10th and 15th patient was quiet except for the two periods mentioned, November 13th and 15th. There was no beating of the head except occasionally for a few moments.

No. 14, November 24th.—Patient was rather excited from 8.30 p.m. of November 23rd onward. Passed clear amber urine at 11.30 p.m., and at 1.25 a.m. the excitement increased, and reached its maximum between 2 a.m. and 3 a.m., being attended by severe beating of the forehead. Afterwards patient quieted down. Passed red urine at 4.30 a.m. (very small in quantity and very dark in colour), then went to sleep. Passed a large quantity (nearly 20 oz.) of dark reddish-brown urine at 8.15 a.m. Was quiet all day after.

On November 25th patient was pretty quiet all day.

November 26th.—Was very much excited during the afternoon from 4 p.m. to 5.30 p.m., beating his head severely. Passed clear amber urine very shortly afterwards. Condition of urine subsequently was not noted.

No. 15, November 27th.—Was excited, beating his head severely from 4 p.m. to 5.45 p.m. Subsequently passed dark red urine.

No. 16, November 28th.—Patient was much excited, beating his head severely from 10.30 a.m. to 11.15 a.m., when he passed clear amber-coloured urine. Was excited again from 1.30 p.m. to 2.45 p.m., when he passed very light red urine. Urine subsequently amber-coloured.

December 3rd.—More or less excited all day, beating himself severely at times for very short periods. Three samples of urine were obtained: the first dark amber; the second a lighter amber; and the third quite pale. No distinct band could be seen on spectroscopic examination in the red or green in either sample. On acidifying and boiling an opalescence was noticeable, but on standing no definite precipitate formed.

It will be seen on reviewing the above attacks that on every occasion self-inflicted violence preceded hæmoglobinuria. The existence of a relationship between the two was early suspected or inferred by the attendants, but it was not until the paroxysm described in the preceding section (page 7) was witnessed that it was decided to make close observations of a series in order to determine more precisely the part played by mechanical injury in their production. It was then found, as the above list illustrates, that in every attack the patient had invariably not only beaten his forehead, but had done so with extreme severity. Thus our own observations of the patient on those occasions showed us that he struck his forehead at very frequent intervals with a heavy thud which was exceedingly repulsive to an onlooker, while the attendants in describing these attacks made use of such phrases as "Was extremely violent to himself," "Never was so excited<sup>1</sup> before," "Beat himself shockingly," and employed other expressions indicative of the severity of his self-administered blows.

It being ascertained, therefore, that extreme beating of the forehead in every paroxysm investigated preceded hæmoglobinuria, the question arises, is the converse of this true? Can the patient beat himself very severely without hæmoglobinuria occurring? Of this we have not been able to discover any incontrovertible evidence. On referring to the series of attacks described it will be seen that on two occasions, November 26th and December 3rd, there is a history of severe beating of the forehead. The first case, however, was unfortunately not fully investigated, since the urine passed shortly after the beating was alone inspected, no note being taken of the next sample of urine, and attention not being called to the

<sup>1</sup> The word "excited" is used to describe the attacks of self-inflicted violence. It must not be understood to mean that the patient is at the same time labouring under an exalted emotional state, for, so far as can be ascertained, he is on these occasions quite free from excitement in this sense of the word.

patient until the urine had been thrown away ; while, as already mentioned, the appearance of red urine does not invariably occur immediately after the beating, there being sometimes, as on November 13th, an interval between the beating and the passage of red urine. On December 3rd, although the beating was severe, its total duration was short, and may thus have been insufficient to cause any considerable discharge of hæmoglobin. These two cases are the only ones which, after careful investigation, we have been able to find of severe beating not observed to be attended by hæmoglobinuria. In the interparoxysmal periods patient habitually strikes his forehead with more or less frequency, but it does not appear that hæmoglobinuria can be caused until severe blows are inflicted for a sufficient length of time. It may be readily imagined that severe beating of very short duration will give rise to a correspondingly small discharge of hæmoglobin, and, indeed, patient's urine has been found on a few occasions to exhibit a trace of proteid, though it has not been possible to attribute with any degree of certainty such traces of proteid to the beating of the forehead. An obvious difficulty in investigating this point arises from the circumstance that it is not possible to measure the amount and duration of the slighter degree of beating of the forehead in quantitative terms, the verbal report of the attendants and our own observation being alone available. It may, however, be mentioned that the traces of proteid which the patient's urine exhibits from time to time in the interparoxysmal periods is, when precipitated, brownish in tint, like the proteid precipitated from red-coloured urine. It is probable, therefore, that these traces of proteid correspond to miniature hæmoglobinuric attacks. The attendants believe that by restraining the patient when he commences to beat himself they can prevent the occurrence of a paroxysm of hæmoglobinuria, as the tendency to beat himself gradually passes off if the restraint is continued, and this belief is probably quite correct. We

have attempted to establish the truth of this surmise by comparing the frequency of the paroxysms when the patient is so restrained with the frequency when restraint has not been carried out. The patient's habit of beating himself is, however, so exceedingly erratic, and the difficulty of obtaining records which are strictly comparable with one another from a number of different attendants is so great, that it has not been possible to place before the reader perfectly satisfactory proof of this assumption, but it may be pointed out that the eight attacks referred to above as occurring in November took place when instructions had been given not to prevent the patient from beating himself, while during the six months preceding October the attendants, as far as possible, prevented him from so doing. Frequently the attendants are able to predict an attack of hæmoglobinuria from the degree of violence which the patient has exhibited; not unfrequently, however, the attack of violence aborts, and no hæmoglobinuria follows.

It having now been made clear that the paroxysms of hæmoglobinuria are causally related to preceding violence, a further occurrence forming a necessary step in the production of hæmoglobinuria remains to be considered. This is the occurrence of hæmorrhage into the loose areolar tissue lying over the frontal bone. It is impossible for the patient to beat himself so severely as he does during his bouts of extreme violence without hæmorrhage occurring, and this escape of blood into the areolar tissue clearly is the first step in the production of the hæmoglobinuria.

Concerning the amount of blood effused, we have already stated in the preceding section that it is small, varying from 1·5 to 3 grammes; that is, of course, assuming, what is in all probability correct, that the hæmoglobin appearing in the urine represents the whole of that effused.

The next step is obviously laking of the blood effused, and for this to happen there must occur a local production

of hæmolysin. The production of hæmolysin in animals brought about by the injection of the blood of another species is now a well-known phenomenon,<sup>1</sup> but after the injection of blood of the same species hæmolysin does not occur.

Nevertheless in the patient whose case is under consideration we have what is probably a unique event, namely, the occurrence of hæmolysis following upon the effusion of patient's own blood into his tissues. Why this should lead to the production of an auto-hæmolysin can only be surmised. Whether it would be possible in healthy human beings for hæmolysis to be brought about by repeated injection of an individual's blood into his own tissues is doubtful, and, in the present state of our knowledge, does not appear likely. In the patient under consideration, however, the conditions are peculiar, since the blood is effused into connective tissue, which is altered as the result of chronic irritation, and in which in particular one would expect to find numerous white blood-cells.

Whether hæmolysis occurs through the white cells exciting or bringing about the production of an "intermediary body," which, with the complement normally present in the blood-serum, determines hæmolysis, cannot be stated, and we have made no experiments to establish this point; but the fact remains that an autolysin is produced, an event of which we cannot find any other instance in medical literature with the single exception of the case described by Michaelis<sup>1</sup> of "post-hæmorrhagic hæmoglobinuria."

In this case a patient had a pelvic hæmatoma, followed a day later by hæmoglobinuria which ceased on the third day, recurring on the seventh day, lasting for four days,

<sup>1</sup> Bordet, "Sur l'agglutination et la dissolution des globules rouge, etc.," 'Annales de l'Institut Pasteur,' 1898, xii, p. 688; 1899, xiii, p. 273; 1900, xiv, p. 257. Also Ehrlich und Morgenroth, "Zur Theorie der Lysinwirkung," 'Berliner klin. Wochenschr.,' 1899, 1; *ibid.*, 1898, 22; *ibid.*, 1900, 21.

<sup>2</sup> "Ueber eine neue Form der Hämoglobinurie," 'Deutsche med. Wochenschr.,' 1901, iv, p. 51.



and then completely disappearing. This case is similar to ours so far as the occurrence of hæmoglobinuria following extravasation of blood is concerned, but in our case the effusion of blood is paroxysmal, and not improbably involves hæmolysis, not of a portion, but of the whole of the effused blood. In the case recorded by Michaelis the production of an autolysin in each paroxysm was preceded by a latent period, during a part of which time preparation was being made of an "antibody." In the patient whose case we are relating a latent period is also sometimes observable, as in paroxysms 11 and 12 in the list on pp. 19—22, though only of short duration. It would appear, therefore, in our case that the autolysin does not exist locally preformed, but that its production is determined by the effusion of blood. How far a mechanical stimulation of the free cells in the subcutaneous tissue of the forehead by the blows is an effective agent in the production of hæmolysin cannot be stated. In our patient no rise of temperature was observed in connection with the paroxysms of hæmoglobinuria, such as occurred in the case of Michaelis, but this was perhaps associated with the much smaller amount of hæmolysis.

The occurrence of hæmolysis serves also to explain another circumstance which has been already referred to, namely, that the beating of the forehead even when severe is unattended with that discoloration of the skin which ordinarily accompanies subcutaneous extravasation of blood. In our patient the usual slow destruction of extravasated blood being replaced by a rapidly occurring hæmolysis, the usual indications of bruising are no longer possible.

Inasmuch as the hæmoglobin of the red cells of the effused blood is dissolved and discharged into the bloodstream, from which it again escapes on reaching the kidneys, owing to the fact that the glomerular epithelium is permeable to hæmoglobin, it follows that the plasma of the patient's blood must itself, during this time, be tinted with dissolved hæmoglobin. If the whole of the effused

hæmoglobin were at the same time present in the patient's blood-plasma, the latter would readily be recognised to be tinted; if, however, the hæmoglobin escaped from the blood-plasma nearly as rapidly as it entered it, no tinting would be recognisable. Our investigations on this point are not complete, so that we are unable to say whether the patient's blood-plasma at the time he is passing hæmoglobin-tinted urine is reddened or not.

Before concluding this section, reference must be made to the form in which the colouring matter of the red corpuscles is present in the urine. During the paroxysms the bulk of the colouring matter is present in the urine in the form of oxyhæmoglobin. A small amount, however, is generally recognisable in the form of a pigment giving a band in the red of the solar spectrum between c and d. Whether this compound is methæmoglobin, or whether it is more properly regarded as acid hæmatin or some other derivative of hæmoglobin, our investigation up to the present leaves undecided. The question is of considerable interest in view of the fact that hæmoglobinuria has been divided into two groups,—that dependent on a preceding oxyhæmoglobinæmia, and that dependent upon an antecedent methæmoglobinæmia.<sup>1</sup> But however this may be, whether, in the case under consideration, methæmoglobinæmia is present at all, or whether, on the contrary, some of the hæmoglobin is altered in the bladder, the amount of the compound present giving a band in the red is extremely small in comparison with the amount of hæmoglobin present.

Finally, reference may be made to the attacks of hæmoglobinuria due to muscular exertion,<sup>2</sup> which are sometimes frequently repeated, and which further investigation may show to be similar to the case recorded above. These cases do not stand in relation to exposure to cold,

<sup>1</sup> Cabot, 'The Clinical Examination of the Blood,' London, 1897, p. 183.

<sup>2</sup> Cf. A. E. Garrod, 'Encyclopædia Medica,' Edinburgh, 1900, pp. 277—286. References to literature are here given.

and are produced only by special forms of exertion, other forms being powerless to produce hæmoglobinuria. Such attacks in the human subject are, as a rule, unattended by symptoms such as accompany the ordinary form of paroxysmal hæmoglobinuria, perhaps because of the small amount of hæmolysis which occurs. In horses,<sup>1</sup> however, hæmoglobinuria due to exertion is attended with muscular rigidity, a symptom which does not appear to have been observed in the human subject; then hæmoglobinuria appears.

#### SUMMARY.

The chief features in the foregoing case may be summed up as follows:

- I. The patient suffers at irregular intervals from paroxysms of hæmoglobinuria.
- II. The paroxysms are preceded by and dependent upon severe self-inflicted violence, causing extravasation of blood into the subcutaneous tissue of the forehead.
- III. Hæmolysis rapidly takes place in the extravasation, the laked hæmoglobin appearing very shortly in the urine, and the amount lost during the paroxysms being, in the attacks studied, equal to that contained in from 1 c.c. to 3 c.c. of the patient's blood.
- IV. The hæmoglobin in the urine is present in the form of oxyhæmoglobin. A small amount of a compound giving in the solar spectrum an absorption band in the red is usually also present.

<sup>1</sup> J. McFadyen, 'Journ. of Comp. Path. and Therapeutics,' March, 1888, and Sept., 1893.

## DISCUSSION

Dr. LOUIS W. SAMBON pointed out that the authors were obliged to surmise that the blows caused an effusion of blood, although there was no evident bruising of the skin. They were also obliged to assume an hæmolysis. He was rather inclined to believe that the violence was an accompaniment of the cause producing hæmoglobinuria. Horses and other animals did suffer from hæmoglobinuria, but it was not due to muscular exertion, as had been believed, but to a specific parasite. The cause of paroxysmal hæmoglobinuria was very obscure, and he would be loth to add traumatism to the already long list of assigned causes.

Dr. J. W. W. STEPHENS drew attention to some of the points of resemblance between this case and cases of blackwater fever due to malaria. In blackwater fever the bands of methæmoglobin were commonly found with those of oxyhæmoglobin, and not infrequently those of urobilin. If the urine in a patient were examined before the appearance of the blackwater it might be found to contain urobilin and albumen, and also traces of a nucleo-proteid as in this case. The only means of predicting an attack was the observation of the occurrence of these substances. Was the doubtful band described by the authors reducible, and, if so, were the bands of reduced hæmoglobin or of hæmatin obtained? In blackwater fever the sediment consisted of yellow-stained matter, part of it being of the nature of granular casts seen in kidney disease and part of so-called clotted hæmoglobin. Hæmoglobinæmia was often not to be detected in blackwater fever on examination of the serum, but it was often jaundiced. The explanation offered by the authors might be the correct one as to a deficiency in the total amount of colouring matter in the form of hæmoglobin failing to give an apparent hæmoglobinuria, but this would not apply to blackwater fever, in which the colour was intense. The isotonic point in blackwater fever was often changed; there was a relative increase of cells with lower isotonic point. The condition of the leucocytes was not strictly comparable in the two conditions.

Dr. VAUGHAN HARLEY thought that hæmoglobin would occur in the urine in any case in which it occurred free in the blood. The case was almost an experimental demonstration of the power of blood to produce hæmoglobinuria. He wondered if the authors were wrong in attributing the escape to hæmolysins; he thought mechanical vibration might so shake the corpuscles as to liberate the hæmoglobin. The presence of urobilin was not of much significance, as it was present before the attacks. He supposed malaria might in this case be absolutely excluded.

Dr. A. E. GABROD thought that just as exposure to cold,

although it was not in any sense the primary cause of paroxysmal hæmoglobinuria, was certainly the commonest exciting cause of the individual paroxysms, so it was not improbable that traumatism might also occasionally act as an exciting cause. He suggested the possibility that the active muscular exertion might in this case be the exciting factor, for in a group of recorded cases the attacks of hæmoglobinuria followed muscular exertion rather than exposure to cold. He thought that the phenomena were more likely to be due to the presence in the blood of patients subject to paroxysmal hæmoglobinuria of a hæmolytic substance than to any special friability of their red blood-corpuscles.

Dr. W. BULLOCH thought that hæmolysis, or laking of blood-corpuscles, might occur in two ways, either directly as by ether, or in a more complex way, mostly by animal products, such as the cobra venom. In the latter usually two substances occurred, one linking on to the other—the immune body and the complement. Was the destroyer of red blood-corpuscles in this case of the first or second class? The case seemed to show that trauma might be a definite cause, but the blood destruction was probably not due altogether to mechanical vibration, but rather to the local beating, which might develop a destructive body, since in this case there was little or no extravasation of blood. In cases of paroxysmal hæmoglobinuria it had been suggested that the poison might be produced locally, as by Ehrlich, for example, in the endothelial cells of the vessel wall.

Dr. WAKELIN BARRATT, in reply, said that scientific proof had been given that the attacks were due to traumatism. The constant presence of urobilin, as in blackwater fever, suggested that destruction of hæmoglobin was occurring. When the urine was passed there was no deposit; after standing, a coloured deposit of phosphates and urates formed. By grinding up blood-cells in a mortar with salt solution the hæmoglobin could not be liberated; this was against the vibration theory. There was no bruising of the skin of the forehead, but there must have been extravasation of blood because of the extreme and continued violence. The theory of the production of hæmolysin from the endothelial cells of the capillaries was of great interest, but evidence of its occurrence in the case under discussion was not forthcoming.



THE DIFFERENTIATION  
OF THE  
CONTINUED AND REMITTENT FEVERS OF THE  
TROPICS BY THE BLOOD CHANGES

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THE great advances made during the last few years in the microscopical methods of diagnosis of malaria and typhoid fever respectively have placed in our hands the power to differentiate, with far greater accuracy than was previously the case, these, the most frequently met with and most important of tropical fevers. Further, by enabling these two to be separated out, we are enabled to investigate, with much greater hope of obtaining at least approximately correct results, the very difficult and all-important question as to whether there are any as yet undifferentiated fevers remaining to be carefully examined and described. The large hospitals of Calcutta furnish an unrivalled field for such an inquiry, and, thanks to the

great kindness of the medical staffs of these institutions (all of whom are officers of the Indian Medical Service, to whom I desire to express my great obligation), I have been able during the last year and a half to examine the blood and carry out the serum tests in about two hundred continued and remittent fevers of all kinds, in both the Presidency General Hospital, which admits European patients only, and in the Medical College Hospital, where the majority of the patients are natives of India. The cases have been taken consecutively, as far as possible, every case being examined when time permitted. Further, I have in my possession clinical notes of the cases and four-hour temperature charts, which have been carefully analysed in order to see how far a study of series of different forms of continued and remittent fevers, as proved by the blood and serum examinations, will enable any rules of value to be laid down for their clinical differentiation. The subject is too vast a one to be treated adequately within the limits of a single paper, but the principal conclusions which have been arrived at may be set forth, and the evidence on which they are based may be summarised.

The nomenclature and classification of tropical fevers adopted by various Indian writers are too varied to be referred to in detail, so it will be best to start with that which Crombie laid down in his address in the Medical Section of the Indian Medical Congress of 1894 (1), which may be taken as a valuable summary of what can be said on the subject of the differentiation of Indian fevers, by means of purely clinical methods, by an observant physician of great experience, mostly acquired in the very hospitals in which I have been recently working. In addition to malarial intermittent and remittent fevers, Dr. Crombie, in his presidential address in Medicine and Pathology at the First Indian Medical Congress in 1894, describes under the head of "Continued Fevers" three certain and two more doubtful forms, as follows :

1. *Simple continued fever*, lasting three to eight days,



and including three fourths of the fevers commonly returned under the head of "ague" in India.

2. *Typhoid fever*, extremely rarely found in natives.

3. "*Non-malarial remittent*," lasting three to six weeks, commonly fatal, and mostly seen in natives.

Doubtful fevers.—4. "*Calcutta fever*" or "*Bombay fever*," being an aggravated "simple continued fever," lasting fourteen, twenty-one, or twenty-eight days.

5. *Low fever*, the temperature varying from  $99^{\circ}$  to  $101.5^{\circ}$ , being very persistent, not affected by quinine, but often cured by a complete change.

No. 3 he regards as being the most important undifferentiated fever remaining to be thoroughly investigated and its organism identified. It was mainly in the hope of separating it, and perhaps other fevers, so as to be able to search for its cause, that the investigation now being described was undertaken. Nearly all the long-continued fevers occurring in the large Medical College Hospital have been examined in the pathological laboratory for a space of eighteen months; and at the same time nearly daily visits were made to the General Hospital at the other end of the town for the purpose of examining all similar cases there. In order to simplify matters as much as possible and to avoid repetition, it will be best to first describe my methods and results, and then to compare them with Dr. Crombie's clinical types.

#### METHODS OF RESEARCH. THE DIFFERENTIAL LEUCOCYTE COUNT.

In addition to the serum tests for typhoid and Malta fever, and the search for malarial parasites, a new method described by me a year ago (2) has proved of the greatest value in this inquiry—namely, the increase in the percentage of lymphocytes in typhoid, and of the large mononuclear white corpuscles in malarial fevers, by which means alone, in the great majority of cases, a correct diagnosis can be arrived at by the examination of stained

blood-films with an ordinary high-power lens. My earlier results have been amply confirmed by the much larger series of cases since examined, while Captain T. H. Delany, I.M.S. (3), has obtained precisely similar results in upwards of one hundred cases examined by him in the Medical College Hospital. The great advantage of this method lies in the fact that the result is in no way interfered with by the previous administration of quinine, as is the search for malarial parasites. As long ago as 1896 (4) I showed, from an examination of one hundred consecutive malarial fevers before the administration of quinine, that in only one third of them could the malarial parasite be found by means of a prolonged search of a single blood-film; and the absence of the parasite from the peripheral circulation in untreated cases has recently been emphasised by Stephens and Christophers (5). In a still larger proportion of cases which have been treated with quinine will negative results be obtained. Thus Maynard (6), working in the Calcutta General Hospital in 1895, found parasites in only 25·7 per cent. of seventy malarial fevers, nearly one half of which had previously taken quinine. As in my present series quinine had been nearly invariably given before I was able to examine the blood, the search for the parasites was negative in the great majority of the cases examined, and no conclusions can be drawn as to the proportion of malarious fevers in the series from the number in which parasites were found. This is also in entire accordance with Captain Delany's recent results (3), for in only 17 per cent. of undoubted malarial fevers examined by him were parasites found, on account of the previous exhibition of quinine, while in over 90 per cent. he was able to correctly diagnose them by the large mononuclear leucocyte increase. It is worthy of note that Captain Delany and myself frequently independently did counts on the same cases at different times, yet never arrived at a different diagnosis. The constancy with which a positive Widal reaction for typhoid has been accompanied by an absence of any large mononuclear

increase, while on the other hand a negative reaction together with a large mononuclear increase has been found in nearly all cases which were either obviously malarial clinically, or which were subsequently proved to be so by their reaction to the quinine test in this large series of cases, appears to me to be in itself conclusive as to the great diagnostic value of the leucocyte count. Stress is laid on this point at the outset, because much of any value in the differentiation and classification of tropical fevers this paper may possess depends on the correctness or otherwise of this new test in addition to the serum reaction. I have already described the method of counting which I have adopted, so need not repeat it here. Briefly, it may be said that blood-films were made by spreading out a small drop of blood on a slide by means of the gliding motion of a needle; they were fixed in alcohol, and stained by Romanowsky's method. Counts were made by working from edge to edge of the middle of the film. Mononuclears, which were as large as or larger than the average polynuclears, only were counted as large mononuclears. From 250 to 500 leucocytes were counted, the smaller number having been found to be quite reliable in most cases after some experience.

The importance of recording the temperature every four hours scarcely needs emphasising, and its value in differentiating between the continued type of many typhoids and the severer forms of malarial remittents will be dealt with later on.

#### TYPHOID FEVER IN EUROPEANS.

It will be well to deal with this, the best known continued fever of the tropics, first, so as to be able to have a standard with which others can be compared. During the last year an unusually large number of cases of typhoid fever have been admitted to the European General Hospital, as will be seen from a glance at the upper curve of Diagram I, so that out of 126 cases of all

kinds examined by me in this hospital during the past year and a half, no less than 50 were typhoid. The notes and blood examinations of these have been tabulated in shorthand, so a brief analysis of the most important points regarding them may be given.

*Age-incidence.*—This is shown in the following table :

*Table of Age-incidence.*

Years	5	5-10	11-15	16-20	21-25	26-30	31-40	Over 40	Total.
Cases	2	3	11	18	7	6	1	2	50

The percentages in each period can be obtained by doubling the figures given, and it will be seen at once that the age distribution of these cases is typically that of typhoid fever.

*Table of Duration of Fever.*

Days	1-7	8-14	15-20	21-25	26-30	31-40	Over 40
Cases	.1 (died)	2	8	19	7	6	7

In the very great majority of these cases among Europeans accurate histories can be obtained, so the accompanying data with regard to the duration of the fever are fairly reliable, although doubtless two or three days at the beginning of some of the milder and shorter cases may have been overlooked by the patients or their relations. In only two cases did the fever last less than 15 days (omitting one case fatal on the 5th day), these being abortive cases which will be referred to again. In eight more cases the fever is recorded as having lasted less than 21 days, one of which proved fatal on the 17th day. Three of them lasted 18 days, one 19, and the other three 20 days. These were mostly mild cases in which an insidious onset may have been overlooked for a time. Of the above cases lasting less than three weeks, all but two were in patients under 21 years of age, typhoid being well known to be milder in young persons. Between the

ages of from 21 to 25 days, nineteen cases, or 38 per cent. of the whole, fall; while seven cases lasted from 26 to 30 days, six cases from 31 to 40 days, and the remaining seven upwards of 40 days, including four cases in which relapses occurred, the longest time having been 69 days. These figures are also characteristic of typhoid fever.

*Clinical characters.*—With the exception of a few mild cases, which did not show very marked symptoms of typhoid fever, but were diagnosed by the serum test, the series was as a whole typical of the disease, and most of them had either been diagnosed as typhoid or were suspected to be such before the blood examination was reported. In thirty-nine of them looseness of the bowels, with more or less characteristic stools, was noted at some period or other of the fever, while thirteen showed constipation. In four hæmorrhage was noted, in one of which it was attributed to coincident dysentery. Characteristic spots were noted in sixteen cases, while in thirteen they were recorded as having been absent. During the hot and rainy season prickly heat is often so extensively present as to make a search for typhoid spots a difficult and uncertain proceeding, but for which they would probably have been found in a larger proportion of cases, for I find they are more frequently detected in the cold weather months, and they are undoubtedly of great diagnostic value in Europeans, even in the tropics. Abdominal symptoms are of the utmost diagnostic importance, as in only eight cases was the abdomen noted as normal, and that usually in an early stage of the disease; while in eight more there was no note on the subject, the clinical records having been scanty in some of the milder cases. In the remaining thirty-four, or 68 per cent., either distension, tympanites, or tenderness, or, most frequently, two or more of these symptoms together, were noted. The spleen was felt below the edge of the ribs in only twelve cases, and the liver in fifteen cases. The pulse was frequently noted to be dicrotic, and bronchial catarrh or congestion of the bases of the lungs also occurred fairly frequently. All

the above points taken together constitute a typical clinical picture of a series of typhoid fever cases, which will serve for comparison with other tropical continued and remittent fevers, and only the important question of the type of the fever curve remains to be considered under this heading.

*The temperature curve.*—The clinical differentiation between a continued and a "remittent" type of fever, although simple enough in well-marked cases, presents difficulties when it is desired to draw a hard and fast line between them. As, however, the separation of the continued type, so characteristic of most cases of typhoid, from the "remittent" type of severe malarial fevers is of the utmost practical importance, an attempt must be made to draw the line somewhere. Bearing in mind that the malarial remittents are caused by the malignant tertian parasites, we should expect a marked remission at least every other day in these cases; while any case in which the temperature varied through a range of only two degrees or less for slightly over forty-eight hours (to allow for some degree of "postponement" in malarial remittents running a favourable course) may be considered to be of a "continued" type. The practical value of this definition will appear presently, and we may now see how frequently this "continued" type occurs in typhoid fever, and how early it is present in a characteristic degree. An examination of the four-hour temperature charts of my fifty typhoid cases from this point of view gave the following results. During the first week of the disease there were admitted twenty-nine cases, of which twenty were admitted on or before the 5th day, and eleven on or before the 4th day, leaving 3 and 4 days respectively of the first week for observation in hospital, yet eight of them showed the "continued" type within that time. During the second week twenty-one more cases showed it, and two others during the third week, and three at later dates. Thus thirty-four out of the fifty cases presented this feature at some time or other in the course of the

disease, the great majority of which showed it well before the end of the second week. On the other hand, in fourteen cases the remissions of the fever were more marked, while in two cases in young children the curve was intermittent throughout. The persistence of a high degree of fever is also an important point to note, for in typhoid cases it is common for the temperature to remain persistently above  $102^{\circ}$  for days together; while we shall see presently this and the "continued" type of fever very rarely occur in acute malarial remittent fevers.

*Death-rate.*—This was 6 per cent., only three cases having died out of the fifty. This points to the very high mortality of 25 per cent. and upwards returned frequently in the British Army in the tropics being due to mild cases being often overlooked.

*The serum reaction.*—The serum reaction was tested in each case with one-day broth cultures in dilutions of 1 in 20, 1 in 40, and 1 in 100 under the microscope, with a time limit of one hour, and only recorded as positive when all active motion of the bacilli had ceased within that time as well as good clumps had formed. Many of the cases were tested more than once, and not infrequently during the later stages a reaction was obtained in a higher degree than in an earlier test, which could only be due to the actual presence of typhoid fever and not due to any previous attack.

*Table of Serum Reactions.*

	- 1 in 20.	+ 1 in 20.	+ 1 in 40.	+ 1 in 100.	Total.
First week . . .	1	2	2	—	7
Second week . . .	7	2	3	10	22
Third week . . .	6	1	6	7	20
Later . . .	5	—	3	10	18
Total. . .	19	5	14	27	67

The above table shows the results of the serum reactions in each week of the disease, and the degree of reaction obtained. The nineteen negative reactions include seven cases

in which no reaction was obtained, although six of them were twice tested, the day of the last test having been from the 19th to the 30th days. In one instance, however, the blood was not examined until the temperature had been normal for eight days, in which time a previously present agglutinating power may have disappeared. (Horton Smith). In the other cases a positive reaction was obtained at a later date. Similarly some of the cases, which at the first test gave only reactions in the lower dilutions, reacted in 1 in 100 at a later date. Reactions were obtained at some period of the disease in 43 cases, or 86 per cent. The cases which did not react have been diagnosed as enteric on account of the clinical evidence of the presence of this disease being very strong, and being confirmed by the leucocyte count, to be described immediately. It will be noted that in the great majority of the cases reactions in dilutions of 1 in 40 and upwards were obtained, which, in my experience, are quite conclusive of typhoid fever, although I have twice met with a reaction in a dilution of 1 in 40 one and two years respectively after a previous attack, but never up to 1 in 100 except during concurrent typhoid fever. The occasional absence of a reaction in typhoid cases is an experience common to various observers, but I have not had any opportunity of making bacteriological examinations for the presence of the group of bacilli which have been found in the so-called paratyphoids in America recently, so cannot say if they should be classed as such or not.

*The lymphocyte increase in typhoid.*—I have elsewhere (2) drawn attention to the value of a marked increase of the percentage of lymphocytes without any noteworthy increase of the large mononuclear white corpuscles, in differentiating typhoid from malarial remittent fevers; and subsequent experience of a large number of cases has amply confirmed, and in some respects extended, my earlier results. My former paper on this subject was largely based on cases of fever in natives, who very frequently do not come to hospital until far on in the disease, so that



the great majority of the cases were not examined until the third or fourth week, when a well-marked lymphocyte increase was nearly uniformly met with in uncomplicated cases. In the present series in Europeans many were examined in the earlier stages, so that they furnish a better evidence as to the diagnostic value of this change in the blood. In the following table the number of examinations in each week of the disease, in which varying degrees of lymphocyte increase were found, is shown in a convenient form for studying the degree and frequency of the change.

*Table showing Lymphocyte Increase in Typhoid.*

First week . .	No increase = 26.			Increased = 46.				Tl.
Number of lymphocytes	-20	20-25	25-30	30-35	35-40	40-50	50	
First week . .	—	—	2	1	1	1	—	5
Second week . .	3	—	7	4	5	4	1	24
Third week . .	4	1	1	2	3	5	4	20
Later . . . .	4	3	1	3	2	7	3	23
	—	—	—	—	—	—	—	—
Totals . . . .	11	4	11	10	11	17	8	72

Of the fifty cases there was no increase in twelve, and an increase in thirty-eight cases, or 72 per cent.

From the above table it appears that the lymphocytes were increased above the normal limit of 30 per cent. in about three quarters of the cases, and this change may even be found in the first week, and in the majority of the cases in the second week, and in almost three quarters of them during the third week of the disease, when it frequently reaches a high degree. Its value, however, is even greater than these figures denote, for as a rule the cases in which it is absent are of a severe type, which can be recognised as probably typhoid fever at a glance, while in the mildest cases it is usually particularly well marked; that is just where it is most wanted. The absence of the lymphocyte increase late in the disease is a bad prognostic sign, while when a severe case in which it has been absent begins to improve, it rapidly appears, so

that there seems to be some relationship between the establishment of immunity and the lymphocyte increase. When in a case of continued fever the lymphocytes are increased, and especially if over 35 per cent. are found, and at the same time there is no marked increase of the large mononuclears (which is so characteristic of malaria), then it is exceedingly likely to be a case of typhoid fever. In cases of malarial remittent fever a similar count may rarely be obtained at the height of the daily rise of temperature; but in these cases the total number of leucocytes present will be very greatly reduced, usually to about 1000 per c.mm.—a condition which I have only seen in malarial and never in typhoid cases. It is important, then, to note the percentage of large mononuclears met with in the series of typhoid cases, so that they may be compared with that of the malarial series to be dealt with presently. The following table shows the results obtained.

*Table of Large Mononuclear White Corpuscles in Typhoid.*

	Normal.			In excess.		Total.
Percentages . . .	—4 .	4-8 .	8-10	11-15	+ 15	
Total examinations .	37	24	4	4	3	72
First and second weeks	—	—	1	1	1	
Third week . . .	—	—	—	—	—	
Later . . . . .	—	—	3	3	2	

From this table we find that in only eleven out of seventy-two examinations were the large mononuclears above the normal 8 per cent., and in only three was the increase found during the first three weeks of the fever, when the diagnosis might possibly have been in doubt. In one of these malarial parasites were found in the blood, the large mononuclears having numbered 18 per cent.; and in another, in which 15·6 per cent. were found, typhoid had supervened on a malarial fever; and in the remaining one there were reasons for believing that the typhoid was also complicated by malaria. The highest number of large mononuclears met with in a typhoid patient was

18 per cent., and malarial parasites were also found in the blood at the same time as a Widal reaction was obtained in a dilution of 1 in 100 (Case 6). In the remaining instances in which over 10 per cent. were found the fever had reached from the thirty-fourth to the seventy-ninth day, and normal numbers of large mononuclears had been found in the earlier stages. It is clear, then, that the occasional high percentage of these corpuscles in the blood of typhoid patients in the earlier stages of the disease usually denotes coincident occurrence of malarial infection, which requires appropriate treatment; while in the later stages there may be some increase after the end of the third week in prolonged cases of pure typhoid, but this can scarcely mislead at such a late period of the disease. A similar late large mononuclear increase has been recorded by Winter in Dublin (10). As we shall see immediately, a marked large mononuclear increase is so characteristic of malarial remittent fevers that its absence should lead to a suspicion of typhoid as against malaria, and that, too, even in the absence of a marked increase of the lymphocytes. I have several times correctly diagnosed cases of typhoid in an early stage by this point, leucocytosis of pneumonia or cerebro-spinal fever, etc., being also absent.

#### TYPHOID IN NATIVES OF INDIA.

The frequency or otherwise of typhoid fever in natives of India was a perennial source of controversy in the pre-Widal days. As the subject is of great importance in relationship to the so-called "non-malarial remittent" fever of Crombie, it must be briefly referred to here, reference being made to a paper in which I dealt more fully with the subject a year ago for further details (7). Dr. Crombie used to hold that typhoid very rarely occurs in natives, and supported his conclusion by the statement that only three cases were returned as such in the large Medical College Hospital in the ten years from 1880 to 1889. By means of the serum test I found twice that number in

the wards of the same hospital at one time, and eleven cases in five months. That number has in the course of eighteen months been increased to twenty-six, together with others in different hospitals and institutions in Calcutta; while reactions in high dilutions have also been obtained with the blood of native fever patients sent me from various parts of Bengal. Lamb has also obtained similar results in Bombay. Clinically they do not differ essentially from the same disease in Europeans, only they tend to be more severe and fatal on account of the late stage of the disease in which they are commonly admitted; while bronchial affections are more common, and diarrhoea less so than in Europeans, the stools being less typical, probably on account of the largely vegetarian diet of the great majority of the patients. The disease is also somewhat more common among children in natives, no doubt on account of their greater exposure to insanitary conditions. More important are the duration and type of the fever for comparison with those of other fevers. Out of twenty-one cases of typhoid in natives, with confirmation by Widal's test in the Medical College Hospital, of which I have full notes, five died before the end of the third week. Of the remainder, all but one suffered from fever for three weeks or more, the exception having only given a reaction in a dilution of 1 in 20, and clinically also the diagnosis of typhoid was not quite beyond suspicion. Nine cases lost their fever between the twenty-first and the twenty-fifth day, and the other six at later dates. These results agree closely with those recorded above in typhoid in Europeans, and lend no support to the view that the disease is commonly abortive and of short duration in natives, although it may very occasionally be so. With regard to the type of the disease, in just half of the cases the "continued" type, as defined above, was observed; that is a somewhat smaller proportion than in Europeans, possibly due to the greater frequency of complication with a malarial element in the case of natives. In the other cases the fever was of a remittent type,

although usually less markedly so than in true malarial remittents. Abdominal symptoms, such as distension, tympanites, or pain, were nearly always met with at some period of the disease—a most important clinical diagnostic feature. With regard to the serum test, reactions in dilutions of 1 in 20 only were obtained in two; in 1 in 40 in six more; and in 1 in 100 in eighteen cases,—a result closely comparable with those in Europeans. Similarly with the leucocyte count: in two thirds of thirty examinations a lymphocyte increase to above 30 per cent. was found, in all but four of which over 35 per cent. were present. On the other hand, in twenty-seven examinations the large mononuclears were not over the normal limit of 8 per cent., and in the remaining three cases they were under 9 per cent., which, we shall see presently, clearly differentiates them from malarial remittent fevers.

The above brief summary is sufficient to prove that typhoid fever is a common continued fever of natives of India, and that it differs in no noteworthy respect from the same disease in Europeans in this country.

#### MALARIAL REMITTENT FEVERS.

We next have to deal with the great class of malarial remittent fevers, whose differentiation from typhoid in their earlier stages is, in many instances, one of the most difficult problems in tropical medicine. In the first place we must define the term “remittent,” and draw some line between it and intermittent cases; for these terms are often very loosely used, different meanings being attached to them by various observers. For instance, in many cases of malignant tertian malarial fever the temperature remains high for some thirty-six hours, and then falls to about normal for a few hours before the same cycle is repeated. This is essentially an intermittent type, and the term remittent should be reserved for those cases in which the temperature remains well above the normal line for some days. In an analysis of the General Hospital records to ascertain

the seasonal prevalence of the different forms of fever, therefore, I adopted the plan of classing cases under the head of "remittent fever" only when the temperature did not fall below 100° F. for two or more clear days; and the following data are also based on a series of cases complying with this definition. I find in my tables twenty-nine acute malarial remittents in the European General Hospital, which both the clinical course and the result of the exhibition of quinine clearly proved to be malarial. Further, they were all examined by the serum test for both typhoid and Malta fever, with negative results in all but one man, who had suffered from a severe attack of typhoid fever in South Africa two years before, and whose blood gave a reaction in a dilution of 1 in 40. All these cases had been liberally dosed with quinine before I had an opportunity of examining their blood, so that the fact that in only a small proportion of them were malarial parasites found in no way negatives their malarial nature. Moreover, as we shall see presently, nearly all of them showed the typical large mononuclear increase of malaria, which fortunately is not masked by quinine, and hence has a peculiar diagnostic value in such a series as this. By analysing them in a similar manner to the former series of typhoid cases, we shall be able to get a clear idea of the diagnostic value in the two fevers of the blood changes; and if these are found to afford sufficient ground for believing that the two diseases have been separated with a considerable degree of accuracy, then a comparison of the course and symptoms in the two series may be expected to furnish us with some useful data for their clinical diagnosis. They may be conveniently considered in the same order as in the typhoids.

The qualifying term "acute" malarial remittents is used above in order to exclude cases of chronic malarial fever—best designated by the valuable old, but comprehensive term, malarial cachexia (which workers in the malarious parts of India desire to see restored to the official nomenclature of the Royal College of Physicians),—for in these

also the remittent type of fever occurs now and then interspersed in the generally intermittent course of the disease. As I have recently showed elsewhere (8), there are certain special blood changes of great importance found in such cases—namely, an extreme reduction in the total number of the white corpuscles, accompanied by a great relative reduction in the polynuclears, with a corresponding increase in the percentage of the lymphocytes as well as the typical increase of the large mononuclears of acute malaria if marked fever is present. These changes are of great prognostic value, and I have suggested that they may explain the great resistance of such cases to ordinary doses of quinine, and also the success I have recently had with very large ones by the mouth or the hypodermic use of the drug in chronic malaria. Interesting as this class of cases are, they fall beyond the scope of the present paper, for they cannot well be mistaken for typhoid or other “continued” fevers.

*Age-incidence.*—This is shown in the following table :

*Table of Age-incidence.*

Years .	5-10	. 11-15	. 16-20	. 21-25	. 26-30	. 31-40	. Over 40
Cases .	2	. 3	. 10	. 4	. 6	. 3	. 1

This shows a very similar incidence to that of typhoid fever, so that no diagnostic import attaches to the ages of the patients in the case of these two fevers.

*The duration of the fever.*—This is of much greater importance, for we have seen that typhoid very rarely runs a course of much under three weeks. In the following table the total duration of the fever both before and after admission is given in the first line, and the time the fever lasted under treatment in the hospital, where quinine was always given in smaller or larger doses, is shown in the second line.

*Table of Duration of Fever.*

Duration of fever in days . . . . .	1-7	8-14	15-20	21-25	26-30	31-40	Over 40
Total duration . . .	3	8	8	2	4	1	3
Fever in hospital . .	12	11	3	2	1	—	—

Here we see a marked difference from typhoid fever, the duration of which exceeded twenty days in four fifths of the cases, and in only 4 per cent. ended within two weeks. Still more marked is the difference in the duration of the fever after coming under treatment, for the majority of the typhoid cases were admitted during the first week of the disease, and therefore had two weeks or more fever in hospital; while in the case of the malarial remittents under treatment with quinine, almost four fifths came to an end within fourteen days of admission, and over one third within one week. This is in agreement with the conclusion I came to over a year ago (7) with regard to continued and remittent fevers in natives (excluding cases of malarial cachexia)—namely, that upwards of 80 per cent. of such fevers which lasted three weeks or more were typhoid fever.

*Clinical characters.*—The chief points in which acute malarial remittents differ from typhoid are mainly of a negative character. Thus in the former, diarrhoea, abdominal distension and pain, rose-spots, and bronchial catarrh are absent or rarely met with. Hæmorrhage from the bowel is very rare, except when dysentery complicates the disease. On the other hand, the spleen is much more frequently and markedly enlarged in the malarial remittents, and the liver is also frequently to be felt below the ribs. A history of chill or rigors or fever on and off for some time previously is in favour of a diagnosis of malarial remittent fever, but it is also not very rarely obtained in cases of typhoid in the tropics, so cannot be relied on very much.

*The temperature curve.*—This is of great importance, for although the remittent type is commonly seen in



typhoid, yet the rises and falls are as a rule much more regular and punctual to the hour in malarial remittents, and also usually of greater amplitude. When the rises occur regularly at some other period of the twenty-four hours than the afternoon or early evening, the case is nearly certain to be malarial. Of even greater value is the fact that in all my charts I can only find one malarial remittent fever in which the temperature remained within two degrees for upwards of forty-eight hours, and at a height of above  $101^{\circ}$  F., unless there was some complication such as pneumonia. Every other case in which this continued type of a high degree was present proved to be enteric fever and not malarial. Of course a similar type is common in pneumonia, but here the presence of leucocytosis will exclude uncomplicated typhoid. As this continued type is most frequently seen during the first and second week of typhoid it is of very great diagnostic value, and has frequently enabled me to correctly diagnose typhoid fever in an early stage of the disease, before other definite symptoms were present; and I look on the establishment of this point, by means of my study of a large number of four-hour charts of continued and remittent fevers controlled by serum and blood tests, as a most important practical outcome of this investigation. The contrary, of course, does not hold good, for, as we have seen, the curve in true typhoid may be remittent, or even rarely intermittent, and may also occasionally show as great regularity of the remissions as in malarial cases. There remain, then, a number of cases in which the temperature curve will not be of any material service, and it is in these that the serum tests and leucocyte counts are of such great value.

*The pulse-rate.*—It is a well-known feature of typhoid fever that the pulse may remain below 100 per minute persistently for days when the temperature is raised to  $103^{\circ}$  or  $104^{\circ}$  F., especially in cases which are running a favourable course. A large proportion of my cases have shown this point in a well-marked degree. On the other

hand, I can only find one chart, out of a number in which the pulse-rate was recorded, in which it remained persistently below 100 per minute in malarial remittent fevers, and this was a very mild one in which the temperature never rose above  $101.2^{\circ}$ . This slow pulse-rate when present is a valuable point in favour of typhoid as against malarial remittent fever, while it is most frequently seen in the mild cases, which are most difficult to diagnose by purely clinical means.

*The malarial parasites.*—As already mentioned, all the cases here dealt with had been saturated with quinine for some days before I was able to examine them, so that the parasites were seldom found in the single slide made on the one or, rarely, two occasions when the blood was tested. When present they were always of the malignant tertian variety, but out of the twenty-nine cases referred to above, in only six of them, or 20.7 per cent., were they detected, Romanowsky's stain being always used. This agrees closely with Captain Delany's results in the Medical College Hospital, Calcutta, under very similar circumstances (3). In two cases, however, the temperature had finally reached normal before they were examined, and in three more it was on its final fall. If these are excluded as extremely unlikely to show parasites, then they were found in 25 per cent. of the remaining cases.

The serum reaction, as already mentioned, was negative, except in one man, who had typhoid fever two years before. That for Malta fever was also negative, except that in one or two cases a clumping in a dilution of only 1 in 10 occurred, as happens occasionally, in my experience, in normal bloods and in those of persons suffering from various diseases other than Malta fever (9).

*The large mononuclear increase in malarial remittents.*—The following table shows the percentage of large mononuclears found in thirty-four examinations of the blood, arranged in the same way as that already given for typhoid cases, except that they are classed in accordance

with the temperature when the film was taken instead of the week of the disease,—the former having an important influence, for, as shown by Drs. Christophers and Stephens (5), the large mononuclear increase becomes less marked as the temperature rises.

*Table of Large Mononuclear Increase in Malarial Remittent Fevers.*

	Normal or slightly increased, 4.				Markedly increased, 30.			Total.
Percentages	—4	4-8	8-11		11-15	15-20	Over 20	
Temp. — 101° F.	0	2	1		7	7	4	21
Temp. + 101° F.	0	1	0		8	3	1	13
Total	0	3	1		15	10	5	34

We see from this table that in only four out of thirty-four examinations were the large mononuclears less than 11 per cent., and in one of these they were increased over that number at a second examination when the temperature had fallen to normal. This is just the reverse of what we found to be the case in typhoid, in only two cases of which during the first three weeks of the disease were over 11 per cent. large mononuclears found, and these were complicated by malaria; so that by the leucocyte count alone the two forms of remittent fever can almost invariably be differentiated. It will also be observed that the highest percentages of large mononuclears are met with in examinations made when the temperature is below 101°, as compared with those made when it is above that point, which is in accordance with the observations of other workers on malaria, as mentioned above.

*Table of the Lymphocytes in Malarial Remittent Fevers.*

	Normal, 23.				Increased, 11.				Total.
Percentages	—20	20-25	25-30		30-35	35-40	40-50	50	
Number of examinations	7	8	8		4	3	3	1	34

From this table we see that more than two thirds of the cases showed no increase of the lymphocytes, while a marked increase was quite exceptional, instead of being the rule, as in typhoid. These two points taken together are of very great value in the differential diagnosis of the two fevers, and will very rarely indeed mislead, if the precaution is taken of examining the blood in the morning during a remission of the fever in cases suspected to be malarial, for it is at the time that the increase of the large mononuclears is best marked.

*The quinine test.*—Before leaving the subject of the malarial remittent fevers we must discuss how far the diagnosis of malarial remittents made by means of the differential leucocyte counts has been borne out by the results of subsequent antimalarial treatment, for unless they will stand this test in patients not yet the subject of marked malarial cachexia, they cannot be relied on. Now in several of these cases the patients had been taking quinine in 10-grain doses three times a day by the mouth for a week or more, with little or no effect on the temperature curve; and this would be held by some to be sufficient to prove that they were not of a malarial nature. This opinion may be true of malaria in some countries, but it is utterly untrue of many cases of malaria as seen in Lower Bengal and other parts of India—a point on which I cannot lay too much stress, as this fallacy has been responsible for much lingering fever and many deaths. During the last fever season at the Calcutta General Hospital, as soon as a large mononuclear increase has been found in cases which have resisted quinine by the mouth, the drug has been given hypodermically in from 5- to 10-grain doses twice a day, the bi-hydrochlorate being used, and injected into the subcutaneous tissues. The results have been admirable, for case after case has fallen to normal in two or three days, some of the charts of which I shall show you presently (Cases 8 to 10). The leucocyte count, then, has come triumphantly out of the ordeal of the quinine test, although in most of these cases no

parasites could be found in the peripheral circulation, and fortunately no opportunity of finding them after death has occurred, although a few years back post-mortems were not very rare in this class of cases, especially when quinine was ordered to be only given when the temperature was below a certain point, with the result that the drug was reduced in direct proportion to the severity of the case, instead of being increased.

*Are there any continued or remittent fevers other than typhoid and malarial?*—As already mentioned, this investigation was started with the object of separating out the known fevers with a view to studying the undifferentiated ones described clinically by Crombie and others, with whom I quite thought that such existed. So far I have dealt with fifty typhoids and twenty-nine acute malarial remittents. In addition to these, six chronic malarial remittents and eleven more malarial intermittents are included in my European series, making a total of ninety-six cases out of the 126 cases examined in the General Hospital. Among the remaining cases we first have a miscellaneous assortment, including cases of phthisis, pneumonia, cerebro-spinal fever, liver abscess, cellulitis, and other local inflammatory conditions, all showing varying degrees of leucocytosis, which in several cases materially assisted the diagnosis. For example, in one case malarial parasites were believed to have been found by the medical officer in charge, but the fever increased steadily in spite of hypodermic injections of quinine, and I was asked to examine the blood. Finding leucocytosis (13,000) and pain over the liver and in the right shoulder, I diagnosed liver abscess, but the supposed parasite had greater weight than the leucocyte count, and the patient was sent on a voyage to Colombo, where his liver abscess was successfully opened. In another case a child suffered from an obscure fever, and two examinations of the blood failed to reveal any evidence of either malaria or typhoid, the case soon after developing into one of tabes mesenterica. In two other cases an irregular fever with some degree of

leucocytosis accompanied dysentery, probably of the amebic type.

When all the above well-known diseases are excluded, what have we left in the way of continued fevers? Practically nothing. Some three or four cases, all in the first twenty examined, when my experience was very limited, remain; and looking at the notes and charts of these in the light of my present experience, I cannot find one which repeated examination would not in all probability have proved to have been either typhoid or malarial. One of these I thought at the time might correspond with the type which Dr. Patrick Manson describes under the term double continued fever, but I have since seen very similar cases which proved to be malarial, and yielded to full doses of quinine. In my last 100 cases I have met with very few doubtful ones, and none which I have any good reason for thinking might be a new and undifferentiated fever, disappointing as it is to have to say so. What, then, are the cases described by Crombie as new continued fevers?

#### "SIMPLE CONTINUED FEVER."

Dr. Crombie holds that three quarters of the cases which are wrongly returned under the head of ague belong to the class he terms "simple continued fever." He describes them as often ushered in with a rigor, followed by high fever, with headache and gastric disturbance, and lasting from three to eight days; but sometimes resembling a mild typhoid and going on for two, three, or four weeks, in which case he calls it "Calcutta fever." They are most commonly attributed to "exposure to the sun." Now the year Dr. Crombie's address before the Indian Medical Congress on Fevers was published I undertook an investigation of a hundred consecutive fever cases in a native regiment stationed in Chota Nagpur; and a microscopical examination of the blood and an analysis of the symptoms convinced me that they were all malarial.

"Simple continued fever," however, has been very commonly diagnosed in the Calcutta General Hospital by those who had the advantage of studying there under Dr. Crombie himself, and several cases quite typically as he describes them, which had been diagnosed under this term, are included in my table of cases. Each of them showed the large mononuclear increase of malaria; several showed a typical tertian character, and they were each cured with quinine; a chart of one will be shown presently (Case 7). I have not yet had an opportunity of examining these cases immediately on admission before they had taken quinine, so am not prepared to state positively that there are not non-malarial fevers of this type; but if so, I am certain they are not anything like as common as Dr. Crombie holds, but hope to be able to further investigate this point before very long. In the meantime some light may perhaps be thrown on the subject by a comparison of the seasonal incidence of the cases returned as simple continued fever and as malarial intermittent fever respectively; for if they are quite different diseases, and especially if the former is commonly due to exposure to the sun, this should be quite different, for the malarial season in Calcutta is the rainy one, when the sun is seldom seen. In the lowest part of the accompanying diagram the cases returned under these two heads month by month during the last three years are shown, the malarial intermittents being represented by the uninterrupted lines, and the simple continued fevers by the broken ones. I find it has been more or less the custom in this hospital to look on short fever cases with any enlargement of the spleen as undoubtedly malarial, and of those without any enlargement as being very probably "simple continued fever," especially if there was no history of chill or rigor. Now one of the first things which strikes a medical man on going to India is the frequency with which typical ague is absent in purely malarial fevers, especially malignant tertians. Further, in first attacks, which will be most frequent at the beginning of the fever season, the spleen will not

yet be enlarged. Malarial intermittents without spleen enlargement will occur in greatest numbers at the beginning and be fewest at the end of the malarial fever season, when they will more frequently show an enlarged spleen due to repeated attacks of the disease. If now we examine the chart of the cases diagnosed under these two headings for the years 1900 and 1901, we see that in both years the two coincide very closely, both in monthly incidence and in number, the only difference being that in the first year the curve of the so-called "simple continued fevers" both rose and fell a month earlier than the malarial cases; this being precisely what might have been expected if all the cases were really malarial in nature, but those without enlargement of the spleen had more frequently been wrongly called "simple continued fever." During the year 1902 it will be observed that this supposed new fever has nearly completely disappeared, especially during the malarial fever season; this change having closely coincided with the promotion to higher spheres of some of the medical officers who had worked under Dr. Crombie, while at the same time greater attention has been paid to the use of the microscope in the diagnosis of the fever cases. This agrees with my former conclusion that nearly if not quite all of these short fevers are malarial in nature, and that "simple continued fever," if it exists at all, is an uncommon disease, and should not be diagnosed until malaria has been excluded by an examination for malarial parasites, or, if quinine has already been taken, also for the large mononuclear increase. It is also worthy of note in connection with the supposed relationship between "simple continued fever" and "exposure to the sun," that the cases returned under this head are fewest during the dry, hot months of March to May, and greatest in the cloudy months of the rainy season. The existence of "simple continued fever" as a separate specific disease still remains to be proved.



### “NON-MALARIAL REMITTENT FEVER.”

Next we come to the fever which Crombie describes under this term, and which he regards as the most important tropical fever whose specific organism awaits its discoverer. It has been a great disappointment to me not to have been able to find this fever to exist at all, as I believed it did when I began this investigation; but on reading over again Dr. Crombie's description of the disease, the mistake into which he has fallen is quite easy to understand in the pre-Widal and leucocyte-count days. To make the matter clear it will be necessary to quote from his writings on the subject, bearing in mind his statement that true typhoid fever is very rare in natives of India, and that only three cases were returned as such in the large Medical College Hospital in the ten years 1880-89. He summarises his description of it in these words:—"This condition, one of persistent high temperature without any marked remission, a distinctly enlarged and congested liver with bilious diarrhœa, a congestion of the back of both lungs, and a low muttering delirium, is generally reached by the eighteenth to the twenty-fourth day. If coma supervenes the patient frequently dies at this period." He also states that quinine has no effect on the fever, and that, although he has seen it in Europeans, yet "it is essentially a disease of natives, and is not common after thirty years of age." With the exception of the absence of the yellow stools of typhoid in Europeans, no doubt owing to the vegetarian diet of most poor natives, this appears to me to be as good a description of typhoid fever as I have seen; yet it is prefaced by the remarkable statement that the fever "is by some considered to be a variety of typhoid fever *notwithstanding its divergence from all the symptoms of that disease!*" It agrees absolutely with the large number of cases of typhoid in natives verified by Widal's test during the last eighteen months in the Medical College Hospital. Further, every such case with the continued type of fever and the absence of

pneumonia, etc., in this hospital has proved on blood examination to be typhoid, so unless Dr. Crombie's fever has disappeared and typhoid taken its place in the last few years, there can be no doubt that his "non-malarial remittent fever" so commonly occurring in natives, who according to him are nearly completely immune to typhoid, is nothing but typhoid in natives.

As already mentioned, I have not been able to find any case of such a continued fever as Dr. Crombie describes in the European General Hospital which has not proved to be either typhoid or malarial. It is worthy of note that he mentions that in his supposed new continued fever "the temperature is generally very high, touching  $104^{\circ}$  and  $105^{\circ}$  for a long part of its course, the daily fluctuations not exceeding  $2^{\circ}$  to  $2.5^{\circ}$  F." Now we have seen that all such cases have been proved by the serum test to be typhoid. This question may also be examined in the light of the seasonal incidence of typhoid as opposed to all other continued and remittent fevers, including malarial remittents. The middle curve of the diagram already referred to shows all the latter cases, and the top one all the typhoid cases, for the last three years in the European General Hospital. The maximum typhoid season is a very definite one, being reached in each year in the dry cold weather and hot weather months (for we have no spring in Bengal) in the first five months of the year, and thus corresponds with the minimum malarial fever season. In the first two years charted there is also a slighter rise in the curve in the rainy malarious months, but this is absent in the last year, when the serum test was regularly used. It would, however, have appeared as usual had not several cases, which had originally been diagnosed as typhoid, been proved by the blood examinations to be malarial remittents. The rainy season small rises of the first two years were probably also due to a few malarial remittents having been wrongly diagnosed as typhoid fever. If now we turn to the curve showing all the other remittent fever cases (all truly continued ones having proved to be typhoid),

we find that the main rise in the curve each year is in the same months as those in which the malarial remittent fevers were most prevalent. This is in exact agreement with the conclusion I have arrived at by means of the blood tests—namely, that the only remittent fever other than typhoid is the malarial remittent. A few cases were returned as “simple continued fever,” but they showed the remittent type, as defined in a previous section of this paper, and they also occurred most commonly during the malarial season. These curves of the seasonal incidence of the remittent fevers other than typhoid, then, strongly support the view that all such cases are malarial, and give no indication of the existence of any new undifferentiated fever in the tropics, the existence of which I now very gravely doubt.

#### LOW FEVER.

Although this is not, strictly speaking, a continued or remittent fever, but rather an intermittent one, yet as it is included under the former term by Dr. Crombie it may be briefly referred to in conclusion. I am glad in this case to be able to agree with him as to the existence of this as a clinically distinct fever, on which the few observations I have yet been able to make may, perhaps, throw a little fresh light. Dr. Crombie well describes it as “a persistent low elevation of fever temperature unaccompanied by any constant symptoms, of indefinite duration, and uninfluenced either by quinine or arsenic. The temperature never falls below 99° F., and rarely rises above 101·5°.” It is met with in Europeans, and causes much depression, and is generally cured by a change of climate or a sea trip. I have, however, several times known it recur on the patient's return to Bengal, even after long leave to England. In my experience also the rise of temperature is always in the afternoon; and never at other odd times, as not unfrequently happens in malaria. I have only had an opportunity of examining the blood in a few cases of this fever, but have always found a marked reduction in

the total number of leucocytes, accompanied by a disproportionate decrease of the polynuclears and a corresponding increased percentage of lymphocytes. Thus the total count may be from 2000 to 5000 per c.mm., while the polynuclears will be reduced to about 50 per cent., or even less, and the lymphocytes increased to 40 per cent., or even more. Now this is just the change met with in cases of malarial cachexia in the absence of active malarial fever, when the large mononuclear increase is not found. On the other hand, we know that when the general health is bad there is a tendency for a reduction of the polynuclears to occur, and it may well be that long-continued exposure to the debilitating influences of a tropical climate may produce an exaggerated condition of this nature. This weakness and want of resisting powers may lead to a loss of complete control by the heat-regulating centres, allowing the body temperature to rise with the afternoon increase of that of the surrounding atmosphere. Against this simple explanation is the fact that I have on two occasions known more than one member of a family affected by this form of fever, which might be held by some to indicate its being of a specific nature; but on the other hand, in one of these instances one of the two sufferers subsequently developed an attack of ordinary malarial fever. The curative effect of a change of air also points to its being a condition of debility rather than a specific fever; and although I am not prepared to dogmatise on the subject with such a small experience, I am inclined to think that the disease is climatic rather than specific, and that latent malaria may play a large part in its causation. With regard to treatment, I have seen the fever disappear, and at the same time the percentage of the polynuclears increase, while oil of eucalyptus was being given—a drug which was suggested to me as useful in increasing the leucocytes by Sir Thomas Lauder Brunton; but my cases are too few to allow me to say definitely that the drug has a curative effect on this form of fever, without further evidence.

## MALTA FEVER.

This concludes the discussion of the different forms of continued fever which have been described as occurring in the tropics, with the exception of Malta fever. I have tested the blood of upwards of 100 continued and remittent fevers by the serum test with the Malta fever micrococcus, but with entirely negative results, with the exception of an occasional reaction in a dilution of 1 in 10 only, which I have given reasons elsewhere (9) for believing to be of no diagnostic value. I find records of cases in the General Hospital in sailors who have recently visited Mediterranean ports, so that our medical officers are familiar with the disease both from this and from their Netley experience; but I find they are nearly all agreed in considering that this disease does not occur indigenously in Lower Bengal, whatever it may do in North-West India. This statement is equally true of Assam in my experience, which is confirmed by that of Major Ronald Ross.

## ILLUSTRATIVE CASES.

The twelve following cases have been selected to illustrate the most important points dealt with in this paper. The nature of the disease, the blood changes found, and the treatment have been entered on the four-hour temperature charts, so that they speak for themselves, and very little description is necessary.

*Typhoid Fever.*

CASE 1.—Clinically, a typical case of typhoid fever. Widal reaction negative on the 15th and 25th day. Lymphocytes increased to 38·2 on the 15th and to 47 per cent. on the 25th day, without any increase of the large mononuclears. The chart shows a continued type of the fever from the 9th to the 11th and up to the 13th and 14th

days of the illness, the temperature not having varied more than two degrees during that period.

CASE 2.—An abortive case of typhoid fever, which was not suspected to be such until a brother and sister were admitted for fever, and I found that all three gave a positive Widal reaction for typhoid, as did two more of the same family admitted shortly after. The fever in this case lasted only 14 days, yet the lymphocyte increase was very marked, 50·4 per cent. being found. In my experience these mild cases, as a rule, show it particularly well.

CASE 3.—This case precisely resembled No. 2, except that the reaction for typhoid was negative on the 7th and 21st days; but the lymphocyte increase was well marked, 48·8 per cent., on the second examination, the large mononuclears not being increased, so I am inclined to regard it as an abortive typhoid, or it may possibly belong to the class recently called paratyphoid. It was one of the very few doubtful cases in the series.

CASE 4.—This case is of interest from several points of view. Clinically, it was for some time regarded as malarial in nature. On examining the blood on the 9th day the Widal reaction was negative, but the lymphocytes numbered 39·6 per cent. without any increase of the large mononuclears, and I diagnosed the case as typhoid on the strength of the leucocyte count. On the 18th day a second examination was made, and now a positive Widal reaction for typhoid was obtained, while the leucocyte count remained practically the same, my diagnosis in the early stages thus being confirmed. I have met with other cases in which I have correctly diagnosed typhoid fever by the leucocyte count before the appearance of the serum reaction, the latter having given a positive result at a later stage of the disease. Another point of interest is the intermittent type of the fever, the

patient having been a child, in which this type is not very rare in typhoid fever.

CASE 5.—A typical very severe case of typhoid, which proved fatal on the 19th day. It shows well the "continued type" of fever, and also illustrates the absence of the lymphocyte increase in very severe cases, which has already been mentioned as being of prognostic value.

CASE 6.—A case of typhoid fever complicated by malaria admitted late in the disease, and giving a serum reaction in a dilution of 1 in 100. The leucocyte count showed 18 per cent. of large mononuclears, which raised a suspicion of malaria, and after some search a few malignant tertian malarial parasites were found. During convalescence a typical attack of malarial fever also occurred. The typhoid symptoms were severe and the temperature of the "continued type," while the lymphocytes showed no increase during the height of the fever.

### *Malarial Remittents.*

CASE 7.—A case of remittent malarial fever showing well-marked fall of temperature every other day, and an increase of the large mononuclears to 16·4 per cent., and yielding to quinine in 5-grain doses every four hours. The case was diagnosed at first as one of "simple continued fever," and I have seen other similar cases which proved on examination with the microscope to be malarial in nature.

CASE 8.—A case of severe malarial remittent fever yielding rapidly to quinine hypodermically. This is the only malarial case I have yet met with in which the temperature remained within two degrees Fahrenheit for two days. Note that at the first examination of the blood, when the temperature was high, 12·4 per

cent. of large mononuclears were found; but three days later, when it had fallen to normal, they numbered 28 per cent.

CASE 9.—A typical case of a malarial remittent fever rapidly cured by the hypodermic use of quinine after the failure of the drug in 10-grain doses three times a day by the mouth. No parasites could be found when the blood was examined four days after admission, when much quinine had been taken, but 15·6 per cent. of large mononuclears were present, which enabled a correct diagnosis to be made.

CASE 10.—Another case of malarial remittent fever diagnosed by the large mononuclear increase, in spite of a positive reaction for typhoid fever due to a severe attack of the disease in South Africa two years before, and successfully treated by hypodermic quinine.

CASE 11.—Another malarial remittent with 21·2 per cent. of large mononuclears and scanty malignant tertian parasites, rapidly cured with quinine hypodermically after failure of the drug by the mouth.

CASE 12.—A case of malarial fever showing a double daily rise of temperature, and very resistant to treatment with quinine. The large mononuclears numbered 16·4 per cent. The patient left hospital unrelieved. No parasites were found on the single occasion when the blood was examined, after much quinine had been taken. These cases of double daily rise are in my experience particularly difficult to treat, and they deserve closer examination.

#### CONCLUSION.

The general conclusion arrived at by the careful clinical and pathological study by modern blood tests of a large



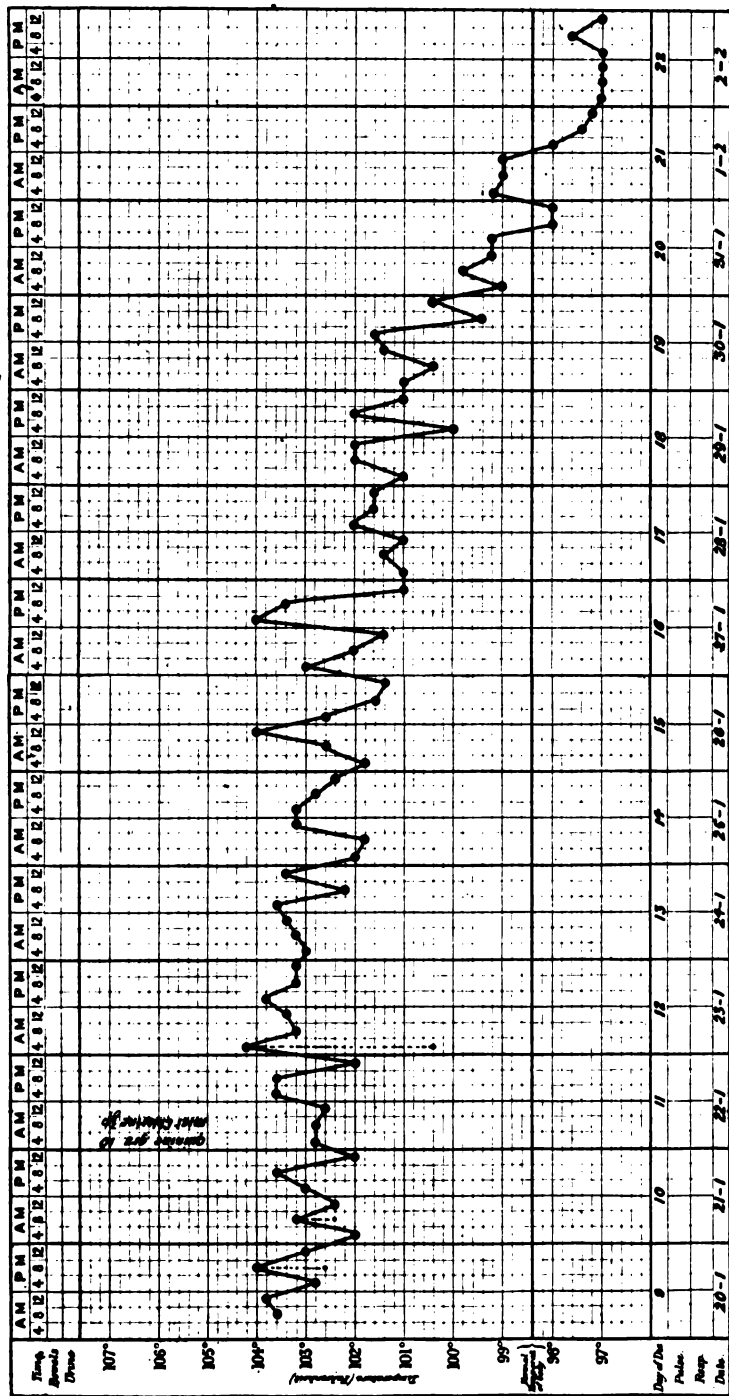
and consecutive series of continued and remittent fevers in both Europeans and natives in the hospitals of Calcutta, then, is that only two forms exist, at any rate of long duration—namely, typhoid and malarial remittents. Further, these can be distinguished in a considerable proportion of the cases by purely clinical methods, of which the temperature curve and pulse-rate, and presence or absence of abdominal symptoms, and the action of quinine, are the most important. The remainder can be differentiated by the serum test or by the differential leucocyte count in all but a very few exceptional cases, the leucocyte count being of special value in the tropics on account of its being available when parasites are absent as a result of previous quinine treatment, and its not requiring a laboratory, which are very few and far between in the tropics at the present time; while it also has some prognostic value.

“Simple continued fever,” if it exists at all as a separate entity, which still remains to be proved, is very rare indeed as compared with malarial fevers. The so-called “non-malarial remittent” in natives has been shown by the serum test to be nothing but typhoid fever. Low fever is distinct clinically, but is probably the result of the debilitating influences of prolonged residence in a tropical climate, including latent malaria, and not a new specific fever. Malta fever does not occur, or at least is exceedingly rare, in Lower Bengal and Assam.

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3. Ibid., March 28th, 1903.
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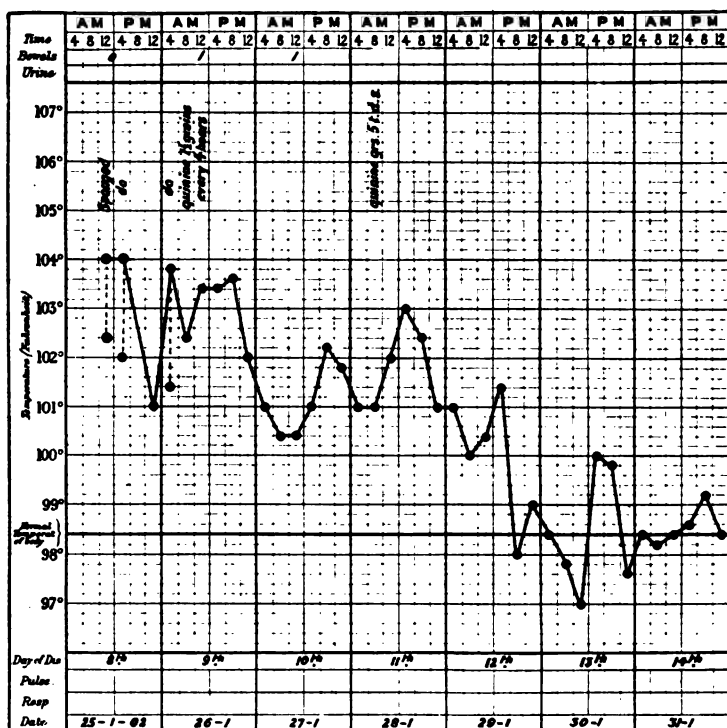
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10. Dublin Journal of Medical Science, October, 1901.
11. Gulstonian Lectures, 1900.



Disease, typhoid fever; J. T—, male, aged 24; admitted January 20th, 1902; recovered.

*Notes of case.*—Clinically typhoid fever, but Widal reaction negative throughout. 18th day—Blood examination, January 26th; Widal for typhoid, -1 in 20; Widal for Malta fever, -1 in 10. Leucocyte count: polynuclears, 58·2 per cent.; lymphocytes, 38·2; large mononuclears, 3·4; eosinophiles, 0·2. 25th day—Blood examination, February 5th; Widal for typhoid, -1 in 20; Widal for Malta fever, -1 in 10. Leucocyte count: polynuclears, 47·8 per cent.; lymphocytes, 47·0; large mononuclears, 5·2; eosinophiles, 1·0.

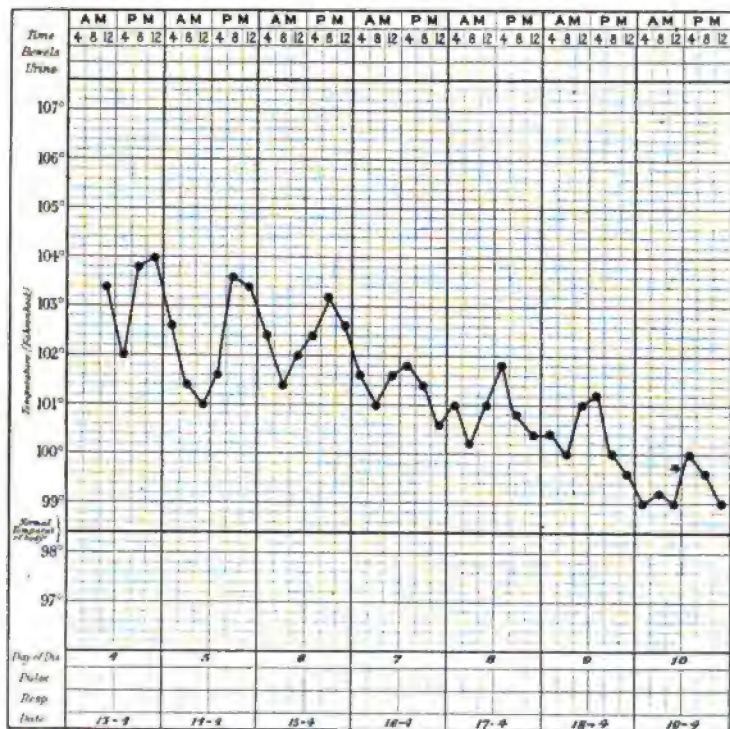
CASE 2.



Disease, typhoid fever (abortive); J. F.—, female, aged 15; admitted January 25th, 1902; recovered.

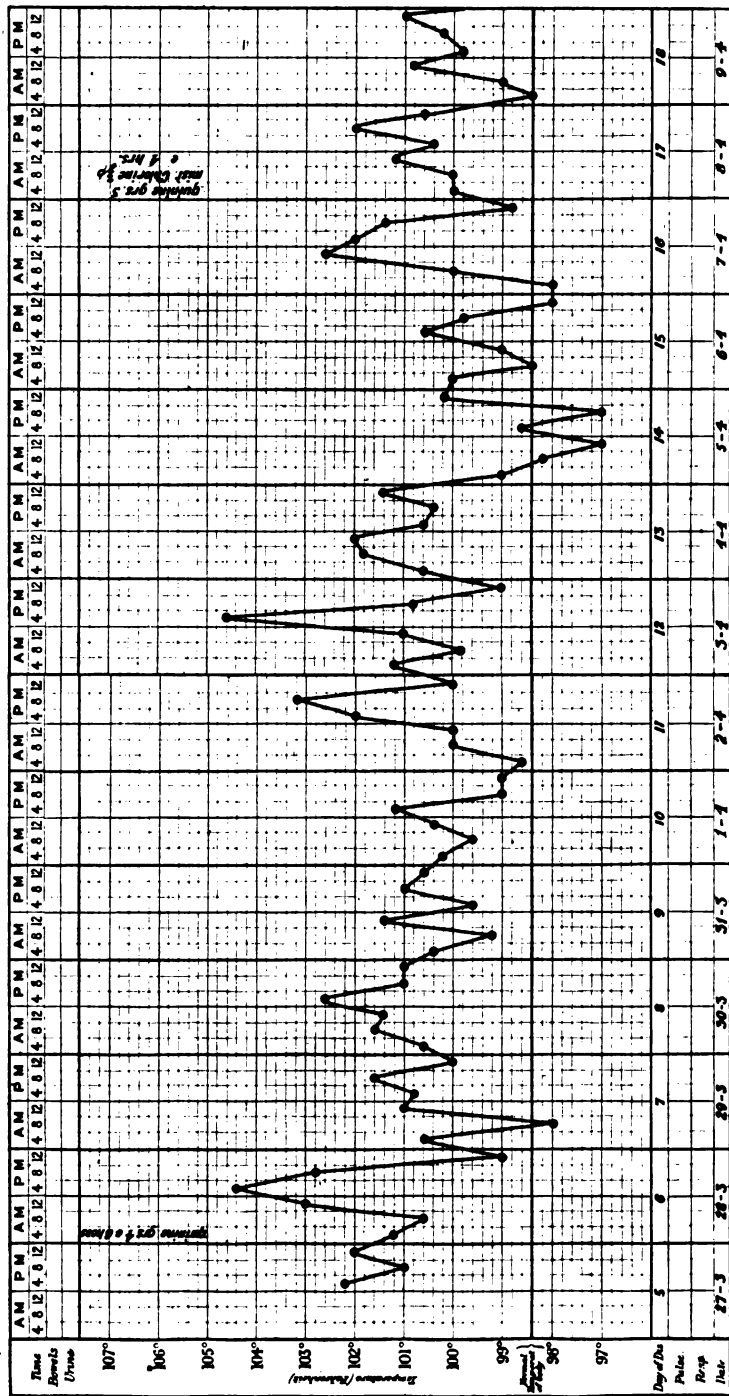
*Notes of case.*—Slight tenderness of the abdomen and some pain. No diarrhoea nor spots. Blood examined February 5th, 1902; Widal + 1 in 100. Leucocyte count, 6250: polynuclears, 42.8 per cent.; lymphocytes, 50.4; large mononuclears, 4.8; eosinophiles, 2.0.

CASE 3.



Disease, ? abortive typhoid or paratyphoid; J. P.—, male, aged 15; admitted April 13th, 1902; recovered.

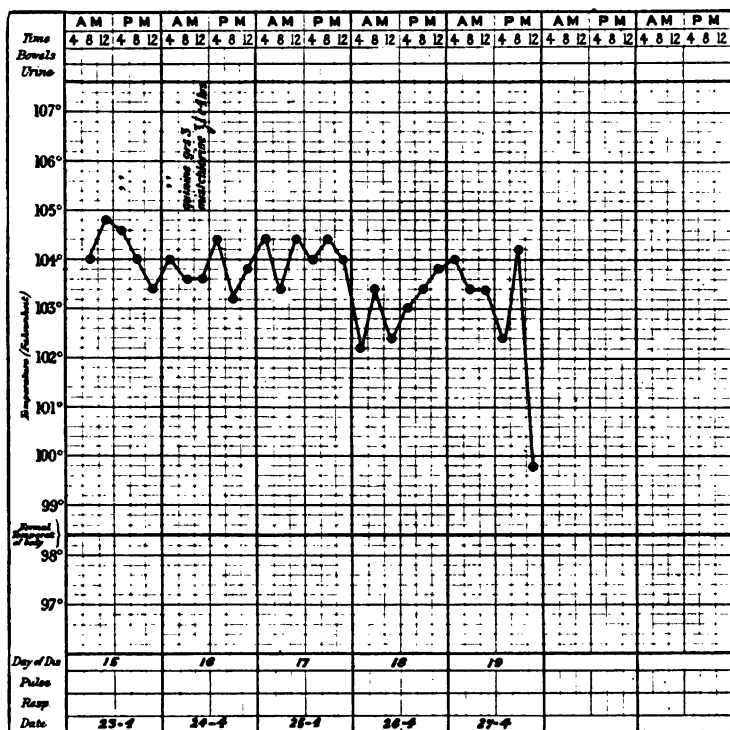
*Notes of case.*—This resembled clinically a very mild typhoid, and was returned as such. *7th day*—Blood examination, April 15th; Widal for typhoid, — 1 in 30; Widal for Malta fever, — 1 in 10. Leucocyte count: polynuclears, 66.8 per cent.; lymphocytes, 28.8; large mononuclears, 3.2; eosinophiles, 1.2. *21st day*—Blood examination, April 30th; Widal for typhoid, — 1 in 20; Widal for Malta fever, — 1 in 10. Leucocyte count: polynuclears, 49.6 per cent.; lymphocytes, 48.8; large mononuclears, 1.6.



Disease, enteric fever; H. H.—, male, aged 9; admitted March 27th, 1902; recovered.

*Notes of case.*—Thought to be malarial at first. Lymphocyte increase found before a Widal reaction could be obtained. 9th day—Blood examined March 31st; Widal, — 1 in 20. Leucocyte count: polynuclears, 56.4 per cent.; lymphocytes, 39.0; large mononuclears, 3.2; eosinophiles, 0.8. 18th day—Blood examined April 9th; Widal, + 1 in 40. Leucocyte count: polynuclears, 56.8 per cent.; lymphocytes, 40.0; large mononuclears, 2.8; eosinophiles, 0.4.

CASE 5.

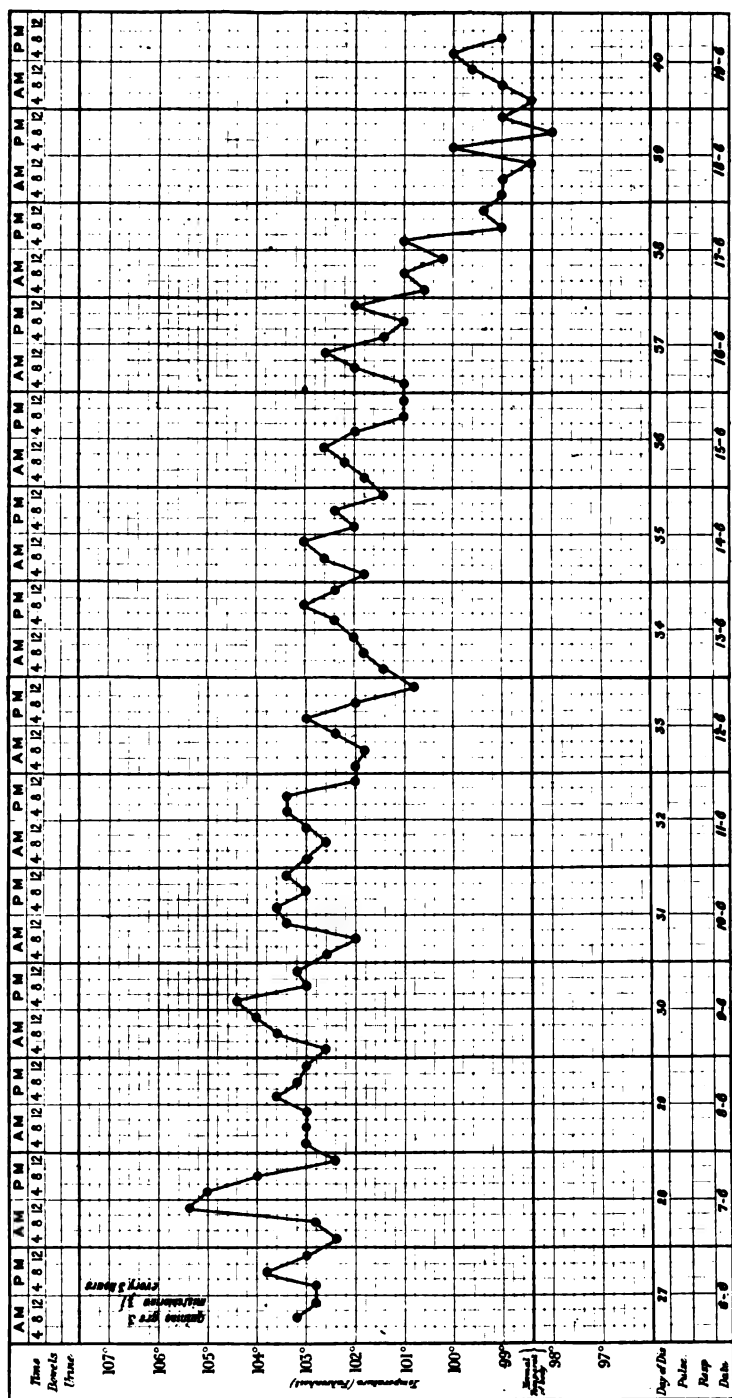


Disease, typhoid fever; V. J.—, male, aged 18; admitted April 23rd, 1902; died April 27th.

Notes of case.—A typical very severe case of typhoid, lymphocyte increase absent. 18th day—Blood examined April 26th; Widal for typhoid, + 1 in 40. Leucocyte count: polynuclears, 79.2 per cent.; lymphocytes, 18.0; large mononuclears, 2.8.

*Leonard Rogers: Fevers of Tropics.*

### CASE 6.

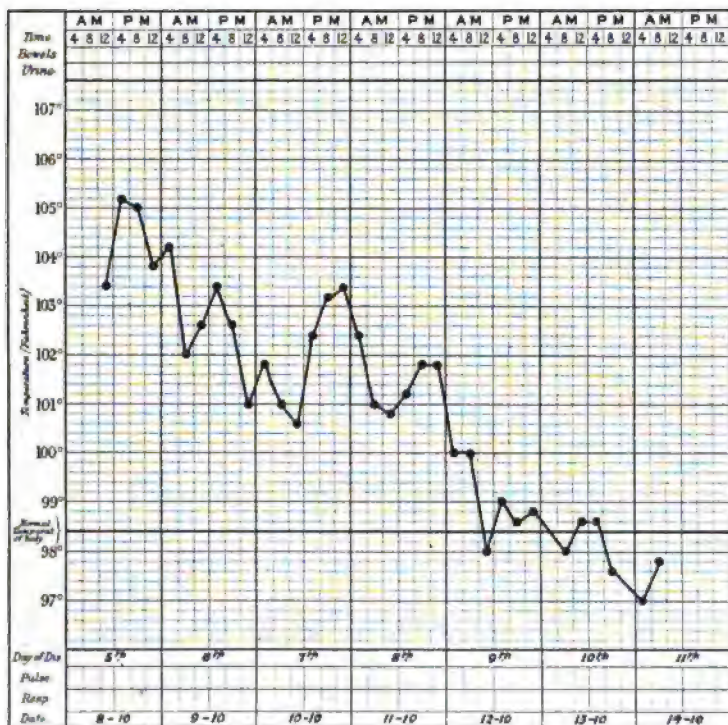


Disease, typhoid fever with malaria; Miss B —, aged 26; admitted June 30th, 1902; recovered.

*Notes of case.*—Blood examined May 7th and 13th. Widal for typhoid, + 1 in 100. Leucocyte count: 28th day—Polynuclears, 60·8 per cent.; lymphocytes, 21·2; large mononuclears, 18·0. 34th day—Polynuclears, 73·2 per cent.; lymphocytes, 14·2; large mononuclears, 11·0. May 7th—Malignant tertian malarial parasites found.



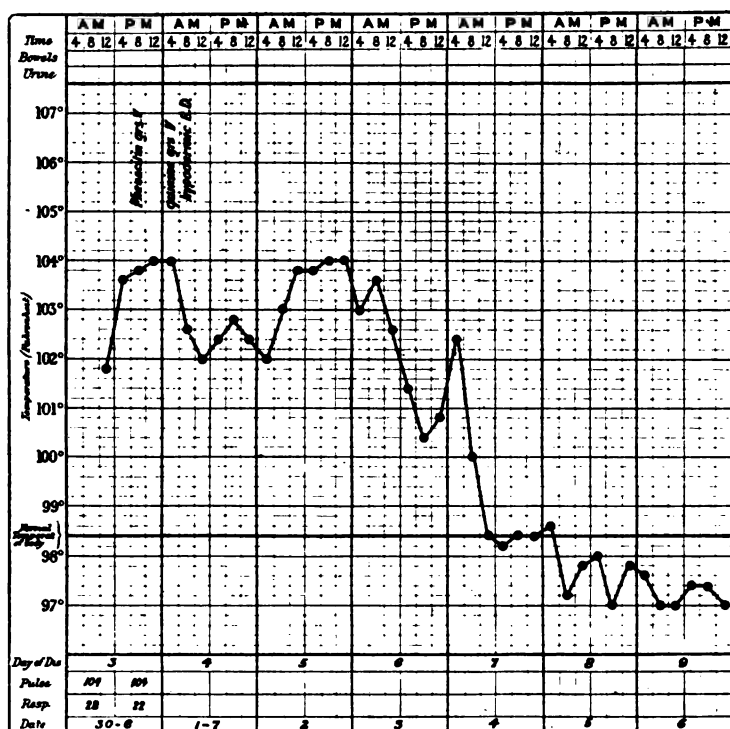
CASE 7.



Disease, malarial remittent fever, malignant tertian ; W. H—, male, aged 17 ;  
admitted October 8th, 1901 ; recovered.

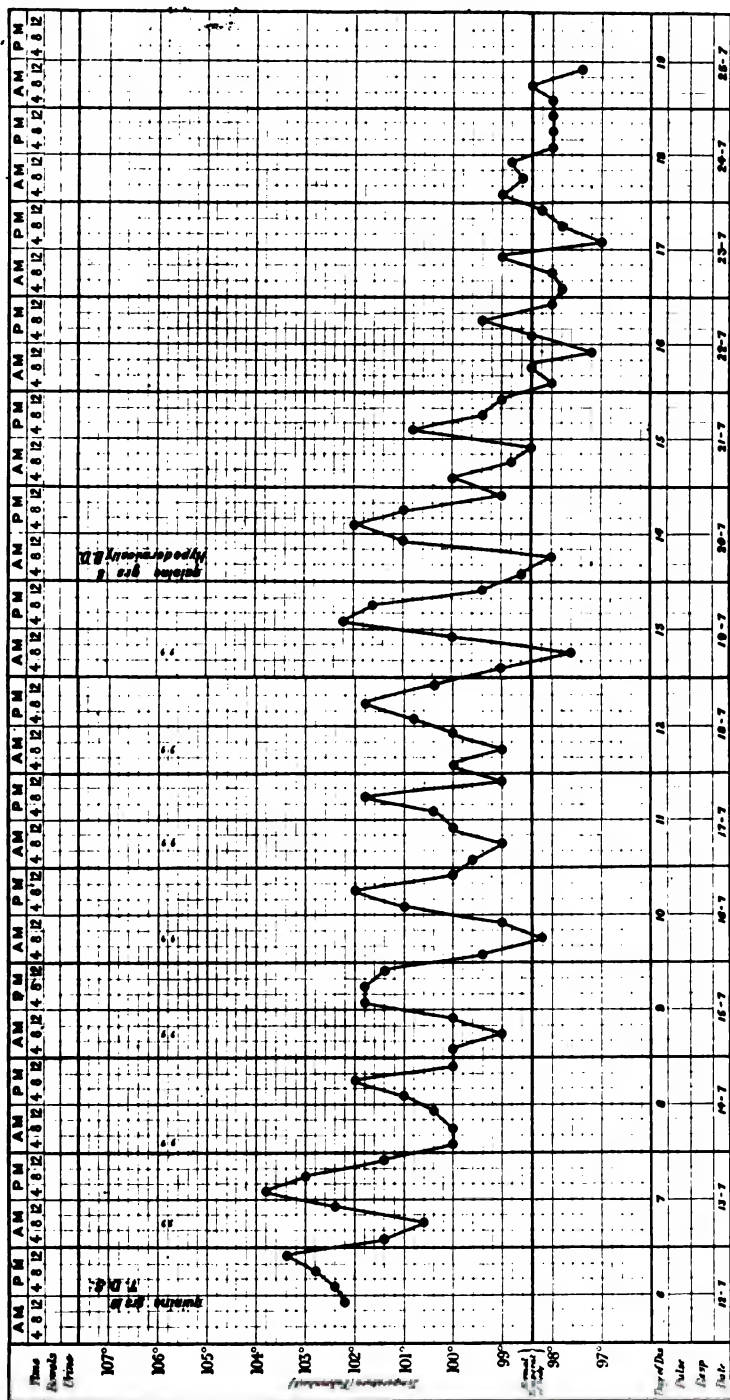
*Notes of case.*—Diagnosed in ward as “simple continued fever.”  
Blood examination, October 13th ; Widal for typhoid, — 1 in 20. Leucocyte  
count : polynuclears, 50.4 per cent. ; lymphocytes, 32.0 ; large mononuclears,  
16.4 ; eosinophiles, 1.2.

CASE 8.



Disease, malarial remittent fever; M. J—, male, aged 20; admitted June 30th, 1902; recovered.

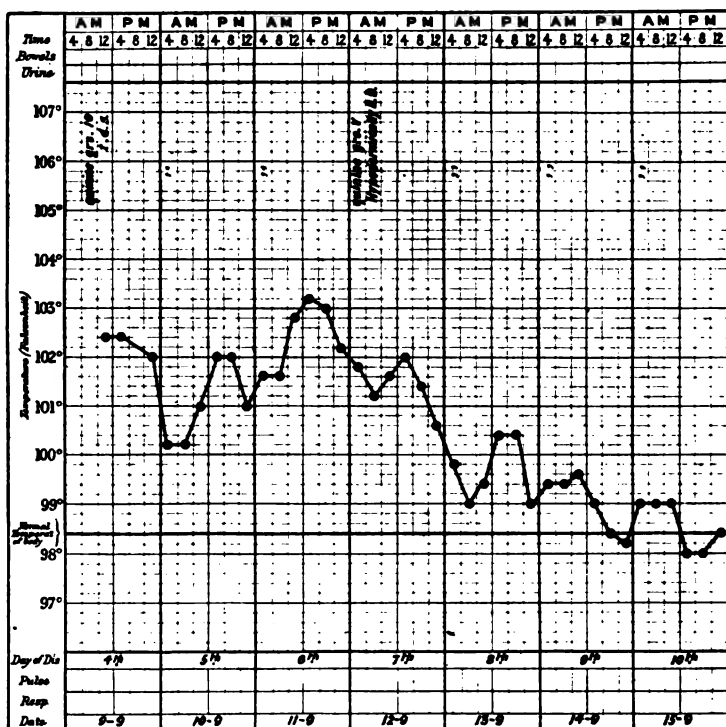
Notes of case.—4th day—Blood examined July 1st; Widal for typhoid, — 1 in 20; Widal for Malta fever, — 1 in 10. Leucocyte count: polynuclears, 63.2 per cent.; lymphocytes, 24.4; large mononuclears, 12.4. 7th day—Blood examination, July 4th. Leucocyte count: polynuclears, 48.8 per cent.; lymphocytes, 27.2; large mononuclears, 23.0; eosinophiles, 2.0.



Disease, malarial remittent fever; R. F., male, aged 28; admitted July 12th, 1905; recovered.

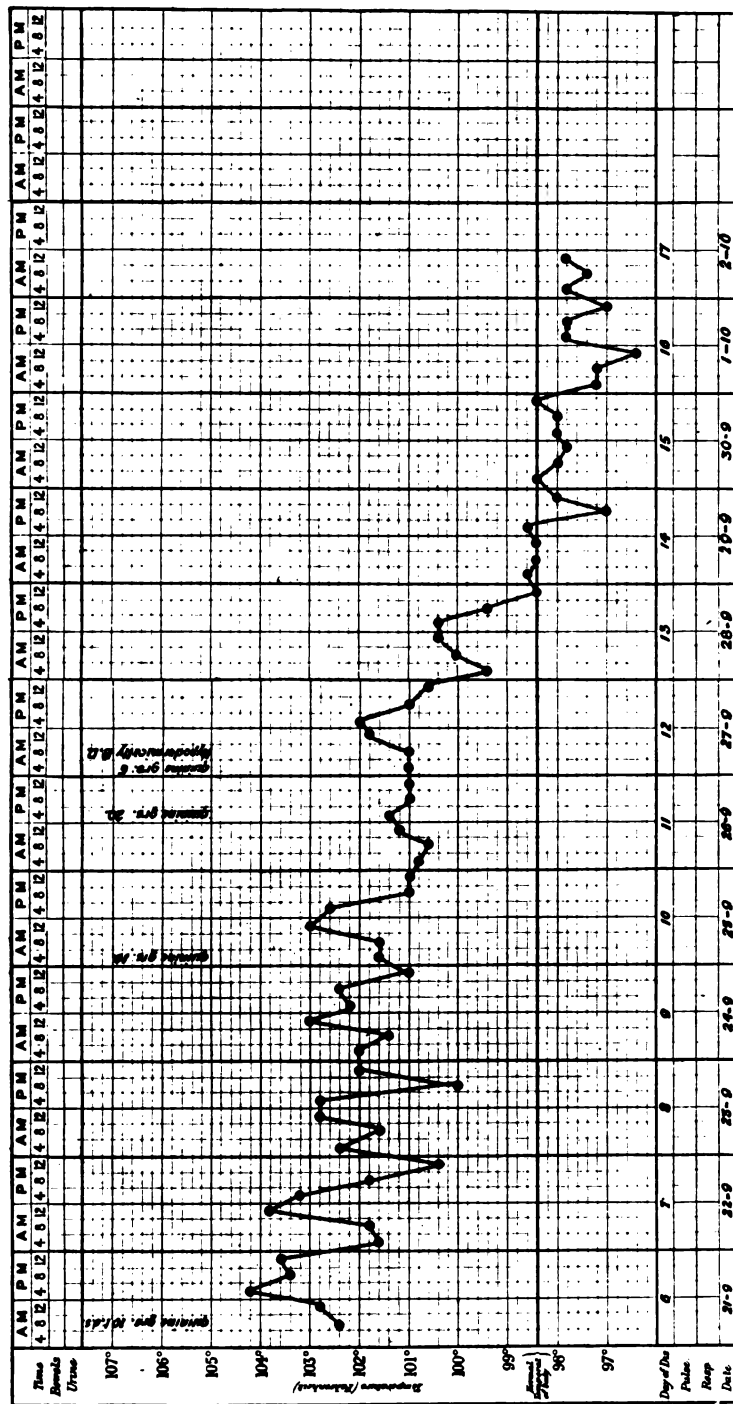
Notes of case.—Cured by hypodermic injection of quinine after the failure of the drug by the mouth. 94th day.—Blood examination, July 16th: Widal for typhoid, - 1 in 20; Widal for Malta fever, - 1 in 10. Leucocyte count, very few: polynuclears, 36.6 per cent; lymphocytes, 48.0; large mononuclears, 15.6; eosinophiles, 0.8.

CASE 10.



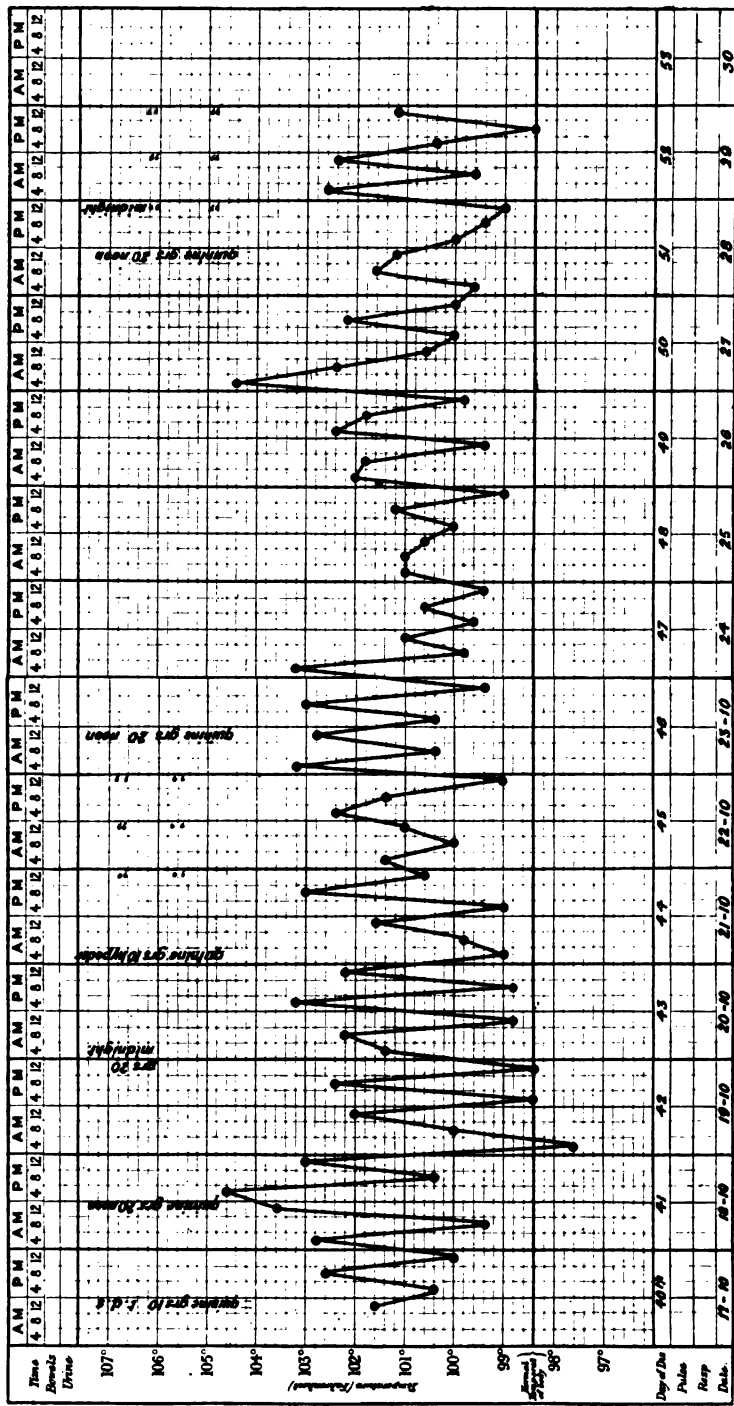
Disease, malarial remittent fever; C. L.—, aged 30; admitted September 9th, 1902; recovered.

*Notes of case.*—Cured by quinine hypodermically. 6th day—Blood examination, September 11th; Widal for typhoid, + 1 in 40; Widal for Malta fever, — 1 in 10. Leucocyte count: polynuclears, 47.6 per cent.; lymphocytes, 37.6; large mononuclears, 14.8. He had had typhoid two years ago.



Disease, malarial remittent fever; L. A., male, aged 32, admitted September 21st, 1902; recovered.

Notes of case.—Cured by hypodermic injections of quinine after the failure of the drug by the mouth. 13th day—Blood examination, September 26th; Widal for typhoid, — 1 in 20; Widal for Malta fever, — 1 in 10. Leucocyte count: polynuclears, 48.0 per cent; lymphocytes, 30.8; large mononuclears, 21.2.



Disease, malarial remittent; C. A., male, aged 30; admitted October 17th, 1902; relieved.

Notes of case.—Malarial remittent, with double daily remission and highly resistant to quinine. Blood examination, October 28th; Widal for typhoid, - 1 in 20; Widal for Malta fever, - 1 in 10. Leucocyte count: polynuclears, 70.4 per cent.; lymphocytes, 13.2; large mononuclears, 16.4.

## DISCUSSION.

Dr. PATRICK MANSON dissented from some of the conclusions drawn in the paper, particularly those relating to the diagnosing of typhoid from an excess of lymphocytes, and of malaria from an excess of large mononuclear leucocytes. Other fevers besides malaria showed the latter excess; as, for example, the fever of trypanosomiasis. When this excess was found it might be concluded that malaria might be present; if it were not found, that it was not present;—a very different thing from saying that an excess of large mononuclears was pathognomonic of malaria. The deductions drawn in the paper were based on Calcutta experience, but this could not be extended to the tropics generally. If the diseases of any one country might be taken as typical of tropical disease, that country was Africa, not India. In regard to the possibly malarial nature of the fever, which he had described many years ago, he said that while in Formosa he had great belief in the specific value of quinine, but when he went to Amoy and encountered this disease, it was broken down, and yet this was not because of the failure of quinine, but because of the failure of his diagnosis. Many kinds of tropical fever which did not react to quinine were not, he was certain, either malaria or typhoid. If quinine were given by the mouth and absorbed, it was quite as effective as if given subcutaneously. The facts advanced in the paper were not, he thought, adequate to justify the sweeping conclusions drawn.

Dr. A. E. WRIGHT said he did not approve of the conclusions, neither did he approve of the methods described in the paper. The alleged increase of large mononuclears in the blood was fallacious, for no arbitrary test of size would distinguish such, as a varying amount of pressure on the films gave differences in apparent size. The percentage of lymphocytes and large mononuclears similarly did not give accurate information, as the polynuclear cells were probably destroyed. It was a point deserving consideration whether quinine would change the relative numbers of leucocytes in normal persons. It would have been desirable to have references to the number of parasites present in the supposed malarial cases to compare with the number of large mononuclear leucocytes. Malaria was probably very rare in Calcutta, and the two remaining fevers, as classified in the paper—namely, typhoid with small mononuclear leucocytes, and the inflammatory conditions with polynuclear leucocytes,—seemed to imply a hasty generalisation.

Dr. Low thought that merely because one particular form of leucocyte was present it was not possible that any disease could be diagnosed; an excess of lymphocytes, for example,

occurred in other diseases than typhoid. It seemed, however, to be certain that an excess of large mononuclear leucocytes did occur with the presence of malarial parasites, and the large mononuclears could, he thought, be recognised with certainty by the microscope. The case described in which there was no response to quinine, but was diagnosed as malaria from the presence of large mononuclears, might have been allied to a form of the new fever of trypanosomiasis, peculiar to Calcutta.

Dr. E. W. GOODALL agreed that the facts advanced in the paper were not sufficient to establish the broad conclusions drawn by the author; it would remain for the observations to be confirmed by others. Serum reactions were not infallible, and possibly the different blood conditions might be equally variable.

Dr. ROGERS, in reply, pointed out that the cases of typhoid described in the paper with an excess of lymphocytes were confirmed with the Widal test. He did not insist that every case with an excess of large mononuclear leucocytes was necessarily malarial; there might be other fevers, like trypanosomiasis, showing the same. In many cases with these present in excess, but with no parasites seen (the patients having been so largely dosed with quinine), the hypodermic administration of quinine gave no reaction. The cases were, no doubt, limited to India, but the observations were made on patients drawn from an area of thousands of square miles, and they were confirmed in one patient from a Boer camp. The large mononuclears were certainly difficult to distinguish, but the doubtful ones were probably not more than 2 or 3 per cent., as Dr. Christophers had pointed out.



# LATENT EMPYEMA IN INFANTS

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HENÓCH, in his 'Lectures on Children's Diseases,' refers to a form of pleurisy which is overlooked because of the meagreness of the pulmonary symptoms. He says that "the 'latency' of the pleurisy is owing not to the nature of the disease, but to the carelessness of the physician;"—because pulmonary symptoms are ill-defined, a proper examination of the chest is omitted. He infers that this remark applies equally to purulent as to simple pleurisy. An empyema cavity may be overlooked also, because it is the second of two such cavities. But there is another class of empyema to which the following remarks refer, latent for other reasons. Pulmonary symptoms may indeed be vague; but in addition, even when a repeated careful examination of the chest has been made, no sure signs of the empyema are discoverable. There are no signs of the disease, or the evidence of intra-thoracic disease is slight, or the lesion may be obscured entirely by its

complications. And it is only a recognition of the whole clinical picture which such a case presents, and of the nature of those obscure physical signs which may arise, that enables a diagnosis to be made at all. These cases, which are occasionally met with in practice amongst infants, are characterised by the occurrence of a small sacculated empyema, generally situated at one base, and beginning insidiously, giving rise to progressive wasting anæmia, and to secondary complications of a grave nature. They sometimes reach the post-mortem table without a suspicion of empyema having been raised, while at other times the question of an empyema has been suggested, and has either been given up, or has led to unsuccessful exploratory puncture. It is the purpose of the present paper to present the most noticeable features of such cases, in the hope that these may less frequently be misconstrued. Their peculiarities will be brought out by considering them under the following heads :

*The symptoms and diagnosis, classified thus :*

1. The onset and general symptoms.
2. The physical signs in—
  - (a) An uncomplicated case ;
  - (b) A case with secondary pulmonary complications ;
  - (c) A case with complications other than pulmonary.
3. Differential diagnosis.

*The effects.*

*The prognosis and treatment.*

*Illustrative cases.*

### THE SYMPTOMS AND DIAGNOSIS.

#### 1. *The Onset and General Symptoms.*

As a general rule the illness of the baby is first made manifest by such common symptoms as languor, peevishness, loss of appetite, occasional diarrhœa or vomiting, and anæmia. If there are symptoms pointing to disease of the

respiratory organs—and such symptoms may be present, though in uncomplicated cases never well marked,—they will usually be a simple dyspnoea and an occasional cough. There is no cyanosis, and the respiratory distress is not of an anxious type. No anxiety is expressed on the face, and no inspiratory dyspnoea is present. The facial aspect is rather that of placid acquiescence in a doleful necessity, and the dyspnoea is largely a simple slight tachypnoea. The pallor, which gradually increases, sometimes has to a slight extent that characteristic yellowish tinge which Dr. Eustace Smith points out as being so characteristic of pleuritic disease in infancy. An irregularly raised temperature is the rule, though not a necessity. In any case which is under observation for several weeks the temperature is almost always high ( $102^{\circ}$  to  $104^{\circ}$ ) every now and then, even though for so long a time as a week it may not rise above the normal. Persistent rapidity of pulse is sometimes noticeable, though occasionally it is remarkable how the pulse-rate does not rise until some serious complication occurs. Clubbing of the fingers is seldom seen; I have only seen it in one case. Progressive loss of weight is a striking feature of the complaint, and great emaciation is often observed. The degree of wasting is dependent upon the chronicity of the disease. Sometimes the early advent of a serious complication leads to death before any extreme degree of emaciation has arisen. This is especially likely to happen with purulent pericarditis, one of the commonest complications; it is commoner with an empyema at the left base. But, as a rule, a fatal complication does not arise till symptoms have been present for some time, and until considerable wasting has occurred. Progressive wasting in a baby with anæmia and languor, in the absence of any sign of tuberculosis or chronic intestinal derangement, should always arouse suspicions of pent-up pus. And having first excluded, as far as possible, purulent otitis media, a latent empyema should be thought of.

## 2. *Physical Signs.*

(a) *In an uncomplicated case.*—The physical signs are probably never very obvious. Only rarely is there a history of sudden onset with indications definitely pointing to an antecedent pneumonia. If these cases are ever the results of an ordinary empyema becoming partially absorbed, this must be a rare event, for there is no evidence in favour of such a view of their origin. It is rare to have a complete absence of abnormal objective signs of disease in the chest; but this may be observed. When, as is usual, signs are present, they have the following characteristics:—(1) They are not well marked; (2) they vary, often from day to day; and (3) a little impairment of resonance to percussion is sometimes the only sign present. To consider each of these characteristics in detail:

(1) *The slowness* and consequent obscurity of the signs are due to several causes. They depend upon the size of the empyema, its chronicity, and its site. The pulmonary system, as it were, accustoms itself to the presence of the small loculus of pus. These sacculated empyemas may occupy any position in the pleural cavity. But there is one common position for them, and two rare ones which give rise to special difficulties. The commonest situation is at the extreme posterior base in the vertebral groove. The two rare situations are interlobar and on the diaphragm. The latter is less infrequent than the former of these. An apical empyema is excessively rare, and its physical signs hardly conform to the variety now under consideration. With regard to the position at the posterior base, the peculiar difficulties which may lead to an oversight of the lesion exist on both sides. For on the one side is the liver, giving rise to some impairment of resonance; and on the other the stomach, perhaps at the time of examination somewhat distended by flatulence, giving a resonant note

to the base of the left chest. Fortunately, as a rule, the impaired note resulting from the empyema extends over a larger area than that actually occupied by the collection of pus in the pleura. Why this should be so is difficult to explain precisely, but it is a point of considerable clinical importance; reference will be made to it later. To diminish the risk of overlooking a latent empyema in these regions, repeated examination of the patient should be made. This is especially important at the left base, because here an impairment of resonance, missed on one occasion on account of some flatulent dyspepsia, often present in these cases, may be noticed on another when the stomach is in a more normal state. With regard to the interlobar site, when a collection of pus occurs in the region of the interlobar septum, it usually presents also on the surface of the lung along the line of the septum, or at all events almost always affords some impairment of percussion resonance along this line. A slightly impaired note in such a region can only be appreciated by a careful comparison of the two sides, care being taken that the scapula and scapular muscles are exactly in the same position on the opposite sides when the comparison is made. When the empyema is under the diaphragmatic surface of the lung, physical signs of the lesion are usually absent. It is almost impossible to discover it either from signs or by exploration. Sometimes, perhaps, a little impairment of resonance to percussion is given to the basal region on the affected side, and on the right side some downward displacement of the liver may be detected, or on the left of the spleen. The liver, indeed, as well as the spleen, may be found abnormally below the costal margin in any variety of basal empyema in an infant. And this, associated with an observable difference between the action of the diaphragm on the two sides, may be a helpful sign. Naturally it is more likely to arise in a diaphragmatic empyema than in the other forms. But on account of the small size of the empyemas now under consideration, this sign can be of little value, especially when one con-

siders the definite enlargement of the liver, fatty or toxic swelling, which is not infrequent in rickety or ill-nourished babies, as well as the relatively large size of this organ in infants. The spleen, too, may be not only displaced, but also, associated with the retention of a collection of infective material, slightly enlarged. And to differentiate between slight enlargement or slight displacement of this organ in patients of so small a size is well-nigh impossible.

(2) *The variability* of the physical signs from day to day depends upon a number of somewhat doubtful factors. This characteristic is of great diagnostic importance, and an appreciation of this fact alone should lead to repeated examination of the patient. It has already been shown that under certain circumstances one cause of this variability is the condition of the stomach. Another cause, to be dealt with later, is the occurrence of secondary pulmonary complications, especially pulmonary collapse. But apart from these there is probably another causal factor to explain this variability. The alteration in the physical signs from day to day must be due partly to a varying condition of the superficial pulmonary tissue. The elasticity of a baby's lung is greater than that of an adult, but the exact degree of aëration of the superficial alveoli in the debilitated infant with a small localised empyema, and, perhaps, a little concomitant bronchitis, is a condition extremely likely to vary.

(3) *Slight diminution of percussion resonance*, with the accompanying feeling imparted to the percussed finger, is the most important sign. It has already been pointed out that this impaired resonance is not always from day to day exactly the same in either extent or degree. At one time it may be noticed all over the back, while at another limited to one region, and at times even the area of impaired resonance may disappear altogether. It has also been shown what peculiar obstacles sometimes militate against its discovery. The importance of gentle percussion cannot be emphasised too much ; for if the percussion

be too heavy, the pulmonary resonance beneath entirely masks an area of slightly diminished resonance often extending over a wide area, fairly easily discoverable by light percussion and a careful comparison of the two sides. That the impaired resonance generally extends beyond the limits of the sacculated empyema cavity has been stated already. One explanation of this, suggested above, is connected with the condition of the underlying lung. But besides this another cause sometimes explaining it is connected with the condition of the neighbouring pleura. This may become secondarily diseased. Occasionally, for example, universally adherent pleura is found associated with such localised empyema; or thickened pleura may be found. Rarely an empyema of this kind gradually develops well-marked dulness, perhaps with other definite signs, over a small area. Then it is no longer so obscure.

*Other abnormal physical signs*, when present, are important, but usually they are not definite enough to be of use in the diagnosis. It must be remembered that they may obscure a correct diagnosis rather than aid in it, unless the observer has been led to suspect a latent empyema from symptoms and from the general condition of the patient, or from a discovery of the signs already mentioned. Weak tubular breathing, diminution of breath-sounds or of vocal resonance, do not come under this category, however; but unfortunately, with the exception of diminution in the loudness of the breath-sounds, which is sometimes noticeable, these signs are rarely present, otherwise the empyema would not so often remain hidden. A slightly higher pitch of the breath-sounds on the affected side may occasionally be noticed, but it is a sign upon which it is impossible to place much reliance. If any adventitious sounds occur, they are usually very scanty and, unless a definite complication arise, limited to the affected side. An occasional hard medium-sized crepitation, probably of pleuritic origin, may sometimes be heard.

When indications such as have been described above

suggest the probability of the existence of this lesion, an attempt to settle the diagnosis must be made by exploration. This question of exploring will be dealt with under the head of treatment.

(b) *The physical signs in a case with secondary pulmonary complications* render diagnosis still more difficult than in an uncomplicated case; for the symptoms of the complication frequently obscure, or, at all events, distract the attention from, those indications of the original lesion which may exist. The secondary pulmonary complications which sometimes occur include pleural adhesions already dealt with. Besides this, many others may arise. Some bronchitis is occasionally a complication. This may be general, or there may be a few medium-sized bronchitic adventitious sounds limited to the affected area. If any bronchitis is present, it is not infrequent for these infants to develop areas, often quite large in extent (half a lobe or more, for example), of tubular breathing, with well-marked dulness and increased vocal resonance. This is almost certainly due to collapsed lung, for frequently such signs last only for a short time, and again reappear. But areas of consolidation may be due to pneumonia as well as to collapse. Occasionally these are of a chronic nature. Such complications add peculiarly perplexing elements to the diagnosis of the true origin of the condition. "Terminal broncho-pneumonia" may arise, too, as so often happens in a chronic wasting disease in an infant.

(c) *The physical signs in a case with complications other than pulmonary.*—When a serious complication has arisen, such as purulent meningitis, pericarditis, or peritonitis, a correct diagnosis of the exact origin of these disorders is of little avail for the patient. Sometimes the patient is not seen by the physician until such a complication has arisen. But the life of the patient is more likely to be saved if, as must be possible sometimes, a correct diagnosis of the exact nature of the case is made. Recovery after operation from empyema and purulent pericarditis is not unknown (see E. G. Davidson in 'Med. Press and Circ.,'



London, 1891, ii, p. 244). A just appreciation of the possibilities, both as regards diagnosis and treatment, will probably save some of these cases. The difficulties of diagnosing purulent pericarditis in such cases cannot be entered into here (see Still,<sup>1</sup> Batten,<sup>2</sup> and Coutts<sup>3</sup>).

### 3. *Differential Diagnosis.*

(1) *From marasmus.*—The commonest error made in these cases is to rest satisfied with a diagnosis of marasmus. There is some excuse for this mistake, not only on account of the obscurity of the pulmonary symptoms, but also because there is often some diarrhœa, and sometimes occasional vomiting too, associated with this state. The points which should arouse suspicion of there being such a cause for the wasting, etc., are—in the first place, the severity of the digestive derangements is not in proportion to the severity of the general symptoms; the rapidity of wasting and the general aspect of chronic illness are greater than one would be led to expect from the amount of diarrhœa. Constant diarrhœa, and still more constant vomiting, are uncommon in these cases. Moreover the appetite often remains good although wasting continues, whereas in marasmus from intestinal origin appetite is usually lost or capricious. Again, at some time or other during the prolonged illness, and usually frequently, the temperature will be irregularly raised, occasionally reaching 103° or even 104°. Now, although in acute diarrhœal affections of infants high temperature is common, in the majority of cases of simple chronic marasmus the temperature is seldom raised above the normal, and is, in fact, more commonly subnormal. If the temperature does become raised upon some exacerbation of intestinal disorder, it will seldom rise above 100° or possibly 101°. It is only rarely, sometimes when the terminal stage of

<sup>1</sup> 'Brit. Med. Journ.,' 1901, vol. ii, p. 606.

<sup>2</sup> Ibid., 1901, vol. ii, p. 605.

<sup>3</sup> 'Edin. Med. Journ.,' Sept., 1902.

gastro-enteritis is associated with pyrexial general toxæmia and nephritis, or sometimes when severe secondary lung disease has arisen, that a higher temperature is recorded. In the latter condition great difficulty occurs, and occasionally it is almost impossible to diagnose a case of marasmus with secondary pulmonary disease from a case of wasting due to latent empyema in which disease of the lung has secondarily arisen.

(2) *From tuberculosis*.—Another almost equally common mistake is that of attributing this condition to tuberculosis. The difficulty of differentiating some cases of latent empyema from tuberculosis is very great. But from the picture of the symptoms given above, it will be noticed that the physical signs do not conform well with those of pulmonary tuberculosis. Thickened pleura of tuberculous origin might, indeed, lead to some such signs, but in an infant such a condition, except complicating pulmonary tuberculosis, is very rare; and should it occur, there is no reason why it should be accompanied by the grave results which ensue. Chronic pulmonary tuberculosis is almost unknown in infancy; but if this disease is present, the features of the case are much the same as in the adult. The signs of the disease would not alter from day to day, but would remain more or less permanently the same, undergoing, perhaps, steady improvement or steady retrogression. If a patient with pulmonary tuberculosis has an evening temperature of  $103^{\circ}$  with any regularity, or over any considerable period, that patient, whether infant or adult, will generally have well-marked and bilateral signs of the disease, and will be going downhill rapidly. But a temperature of this variety may occur with a small sacculated empyema without there being either well-marked or bilateral signs of pulmonary mischief, and without producing a rapidly fatal result. Dr. Emmett Holt<sup>1</sup> publishes a case of this kind, where double undiagnosed diaphragmatic empyema was the cause of a prolonged high temperature having wide fluctuations and lasting for

<sup>1</sup> 'Archives of Pediatrics,' N. Y., Jan., 1902.

more than three months. This case showed many of the characteristics which have been dwelt upon above; amongst others the variability of signs, the ineffectiveness of all treatment, the progressive emaciation, secondary general pleural adhesions, and secondary broncho-pneumonic consolidations of a chronic nature. Similar indications to guide in the differential diagnosis apply to acute caseating pulmonary tuberculosis; whether pneumonic or broncho-pneumonic. The latter disease is comparatively common in infants; it steadily progresses to caseation and softening until the death of the patient; and the signs are bilateral. Other points to which attention may be drawn in the differential diagnosis are connected with the cough. Infants with a small sacculated empyema usually have some cough; often it is of a paroxysmal nature, but it is seldom troublesome. Though infants nearly always swallow expectoration, it is usually possible to tell from the nature of the cough whether it is accompanied with expectoration or not. And in the case of infants with a small sacculated empyema, the cough is generally feeble, infrequent, and purposeless; whereas in acute caseating broncho-pneumonic pulmonary tuberculosis the cough is, as a rule, frequent and purposeful, *i. e.* it has the peculiar characteristics of a cough which either attempts to bring up, or does bring up, expectoration. Moreover it is frequent in caseating tuberculous broncho-pneumonia for some cyanosis and laboured breathing to be noticeable features throughout. Again, difficulty may arise because the gradual loss of flesh may simulate the premonitory stage of general tuberculosis. And if generalised tuberculosis should arise from a primary pulmonary focus, possibly with the remains of old pleurisy, it will often be impossible to diagnose it from a latent empyema, especially if the primary tuberculous focus is near the base. But such a condition is extremely rare in infants. It is commoner in them to get the preliminary wasting of general tuberculosis followed by and terminating with pulmonary signs. And in rather older patients with general

tuberculosis, even when a chronic local tuberculosis in the lungs is the primary lesion, wasting, with symptoms resembling a continued fever, often precedes for a long time any signs of disease in the chest. Whereas with a latent empyema, if the patient is examined repeatedly and with care, physical signs of disease in the chest can usually be discovered in the very early period. As a rule the long delay of the fatal issue, *i. e.* if no serious complication has arisen early, should in itself cast a doubt upon the diagnosis of general tuberculosis when applied to these patients. The yellowish tinge of the anæmia is often a helpful sign; and probably the variability of the patient, shown by an occasional replacement of the settled apathy by a greater sprightliness of manner, and by the occurrence of a slight improvement in the general condition, which raises hopes of being progressive, but lasts only for a day or two, are features better marked in marasmus having origin in a latent empyema, than in chronic wasting from other causes. A weight which is temporarily stationary, or even a little increase in weight, may be associated with such periods of slight improvement. Sometimes when great emaciation has developed the weight may remain the same for as long as several weeks; but this is not peculiar to latent empyema.

The possibility of a latent empyema being associated with tuberculosis must be admitted. Holt ('Diseases of Children,' 1900, p. 1025) says that a small sacculated empyema and adherent pleura may be associated with tuberculous broncho-pneumonia. But in none of the cases of latent empyema I have seen has there been found any sign of tuberculosis.

(3) The differential diagnosis of cases with complications from chronic broncho-pneumonia, or from purulent pericarditis and other such conditions arising primarily or secondarily to diseases other than latent empyema, is usually very difficult. Attention must be paid to the history, course, and general features of the disease, and to a search for signs of the primary disorder.

## EFFECTS.

The secondary effects of a small collection of pus, more or less chronic and inspissated, but probably always containing micro-organisms (generally the pneumococcus) in a loculus formed by the layers of the pleura, differ in no way from a similar collection of purulent material in other parts of the body. Most of these effects have been already dwelt upon in the preceding section of this paper, but for the sake of clearness they may be brought together here. They may be classified under two heads.

1. *Indirect or toxæmic*, the result of the presence of a localised collection of pus.

(a) *General*.—Debility, anæmia, fever, and wasting, with which are often secondarily associated flatulent dyspepsia, diarrhœa, bronchitis, collapse of lung, and other pulmonary complications, and occasionally enlargement of the spleen.

(b) *Local*.—Thickening of the pleura forming the wall of the abscess cavity, inflammation of the neighbouring pleura, giving rise to adhesion between the pleural membranes, localised compression of the lung, chronic inflammation of the lung with fibrosis, in the neighbourhood of the empyema.

2. *Direct or bacterial*, the result of spread of the infective agent either locally or by the blood.

(a) *Locally*.—Purulent pericarditis (and peritonitis).

(b) *Blood infection*.—Purulent meningitis, peritonitis, arthritis, and other pyæmic abscesses (and pericarditis).

This classification of the secondary effects is a somewhat arbitrary one. The pulmonary and pleural complications, for example, may arise sometimes in one way and sometimes in another. In fact, often there is great difficulty in saying under which head they should come. The close proximity of many of these loculated empyemas to the pericardium, the common occurrence of pericarditis as a complication, and the thickening of the parietal pericardium which is sometimes found in the immediate vicinity of the empyema cavity, all lead to the supposition

that this complication arises from the direct spread of the infective agent locally; though possibly sometimes the pericarditis is of a pyæmic nature. With regard to purulent peritonitis, the reverse is probably the case, this complication being generally pyæmic in origin, though occasionally arising by direct spread through the diaphragm.

#### PROGNOSIS AND TREATMENT.

The prognosis is bad; the majority die. The cause of death is usually one of the serious complications—those belonging to the bacterial group. It is doubtful whether these small sacculated empyemas ever completely dry up while the patient makes a thorough recovery. Probably occasionally nature brings about a cure in this way; but one could wish to be more sure that this method of cure occurs with any degree of frequency before attempting to rely upon it. Perhaps many patients who do not reach the wards of a hospital or the consulting room of a physician (though the latter is a rarer event, because these cases are more likely to occur in the badly nourished children of the poor) recover by this method. If such cases, which are not only unrecognised but also recover, exist, it is of course impossible to compute the mortality rate accurately. The fact of practical importance is that the great majority seen by a doctor die. This mortality depends not only upon the infrequency of correct diagnosis, but also upon the difficulties of treatment. The aim of treatment is to cure the condition before any serious complication arises. The case must meet with energy and ever watchful attention for it to have that chance of recovery which exists.

The first question which arises is whether under any circumstance it is well to postpone exploring the chest. An abundance of fresh air with good feeding will do much for these patients. But without doubt, whenever pus is suspected exploratory puncture is called for. Then, in conjunction with its evacuation when found, or after

repeated attempts have failed to find it, the excellent therapeutic measures of "open air," particularly a mild sea air, and "over-feeding" may be employed. This therapeutic principle, as it is now applied to chronic pulmonary tuberculosis, could with advantage be applied to a much larger number of diseases than is at present customary; and this is one of the many disorders in which the adoption of this method will meet with success.

The next question for decision is how often should an exploration be made, supposing pus is not found at first. This depends upon two circumstances: the certainty of the diagnosis and the progress of the case. Holt ('Diseases of Children'), in discussing empyema, says that when the physical signs point to fluid eight or ten punctures may be necessary to decide whether it is present or not. Two or three may be performed at intervals of a day or two. One of the patients I have seen, an infant aged 1 year and 7 months, under the care of Dr. Eustace Smith at the Shadwell Children's Hospital in September, 1900, a patient who had clubbed fingers, was explored on three separate occasions. But the locus of pus was not found until the autopsy. This patient developed, amongst other complications, a chronic broncho-pneumonia. The number of exploratory punctures, then, must vary with the degree of confidence the physician places in the correctness of his diagnosis, and upon the progress that the case is making. If the patient continues to get worse in spite of all treatment, then, so long as a suspicion of the presence of pus in the pleural cavity exists, further exploratory puncture is not only justifiable, but highly expedient.

Having decided that the first thing to do in these cases is to attempt to establish the diagnosis and to localise the purulent cavity, the method and difficulties of exploring are to be considered. Frequently exploration is a matter of no little difficulty. As I have already indicated, the signs often give but slight assistance in arriving at a correct idea as to the situation of the pus. All that can

be done is to examine the patient frequently and take note of the area over or around which abnormal physical signs are most commonly present. This spot must be chosen for the first exploration. The common situation of these pus cavities at the extreme posterior base must be remembered. The difficulty of finding pus by this means when it exists in a small sacculation at the extreme posterior base close to the vertebral groove, or in the supra-diaphragmatic region, raises the question as to whether further measures should be pursued when no pus has been found in a case in which it is felt that some is present. Here, again, much depends upon the certainty of the diagnosis and the patient's progress. The danger of doing damage when exploring in these basal regions is a very real one; this is especially true on the left side. But the operation of removing a piece of rib towards the base and exploring with the finger or probe must not be undertaken lightly, for it is a serious one in a patient of this kind. Upon rare occasions, however, after carefully weighing each point for and against exploratory rib resection, it is obviously a justifiable operation to undertake.

When pus is found, its prompt evacuation is essential. This is best accomplished by the removal of a small piece of one rib. Though in ordinary empyemata in infants an incision is, as a rule, all that is necessary, in these cases where the pus is small in quantity but inspissated, and where the pleural wall of the pus-containing cavity is thick, it is best to proceed immediately to the more formidable undertaking. It is beyond the province of this paper to deal in detail with the treatment of complications. The most important point in their treatment, an obvious one, but one which cannot be emphasised too much, is to remove the primary cause. If the cause has been satisfactorily removed, there is then some hope of dealing with them successfully. But if this cause remains, permanent improvement in any of the symptoms will seldom be accomplished by any means. When some of the severe secondary effects of this disease



have arisen, the patient's state is desperate. But even when the most serious complication has arisen, the case must not be considered absolutely hopeless.

#### ILLUSTRATIVE CASES.

The following six cases were all patients treated in the wards of St. George's Hospital. The disease, which is not common at a children's hospital, is rare at a general hospital. Five out of the six have occurred since 1900; but these are the only cases, in which the diagnosis has been confirmed at all events, since 1896. One patient who died recently in St. George's Hospital, an infant of 18 months, had a prolonged high and irregular temperature for nearly four months. Gradual wasting and anæmia ended in death from asthenia. This patient had throughout slight, obscure, and very variable signs, always limited entirely to the left chest, with sometimes an ill-defined impairment of resonance towards the base as the only sign. The similarity of this case to the one already referred to, published by Dr. E. Holt, was striking in many ways. Several exploratory punctures gave negative results. Unfortunately the diagnosis of a supradiaphragmatic empyema on the left side could not be confirmed, because both operation and post-mortem examination were refused by the parents. Of one or two other cases, seen at the Shadwell Children's Hospital, I have no detailed notes; but the following six examples will suffice to illustrate the condition :

CASE 1.—T. P—, was a male, aged 16 months, who was admitted with a history of having had some wasting and a slight cough for several months. The onset was gradual and insidious. When first seen he was pale, but fairly well nourished; there was no respiratory distress; the respirations were 40, the pulse 132. The signs, which were not well marked, were impaired resonance to percussion, with slightly diminished breath-sounds of

rather a high pitch over the right lower lobe, and, at the extreme base on that side, a few crepitations. The temperature intermitted, reaching  $103^{\circ}$  once, but usually only rising as high as  $101^{\circ}$  in the evening. Except for this temperature, the case did not suggest broncho-pneumonia, but was thought to be debility with pulmonary collapse. Fluid was thought of, but was dismissed because the signs did not become more definite towards the base, vocal resonance was not definitely diminished, and because the signs were transient. The variability of the signs was well marked. About a fortnight after admission the only abnormal sign found was very slight diminution of percussion resonance over the greater part of the right lower lobe. Two days later even this disappeared, only to return in a few days rather better marked. By this time the patient had wasted considerably, and the anæmia had increased. There was no diarrhœa worth mentioning, and on only two occasions did the patient vomit. A small empyema was diagnosed, and an exploration made. But this gave a negative result, and when head symptoms arose, eight or nine days later, although the true nature of the case was suspected, tuberculosis was generally accepted as an explanation of all the symptoms. The post-mortem revealed an old empyema at the right base, with meningitis and pericarditis of quite recent origin. The latter was undiagnosed.

CASE 2.—F. J—, a female aged 2 years, was in the hospital for two months, during which time she had a temperature varying between  $97^{\circ}$  and  $102^{\circ}$ . At the post-mortem examination she was found to have an old loculated empyema at the left posterior base, recent pericarditis, universally adherent pleuræ, and partially collapsed and emphysematous lungs. The empyema was never diagnosed. The onset had been gradual, extending over three months. She was fairly well nourished when first admitted, but subsequently became extremely emaciated and cachectic. The day before she died she

weighed only 13 lbs. The signs varied considerably from time to time; at first, and almost throughout, they were limited to the left side, and generally best marked towards the base. The signs noticed at one time or another were dulness, diminution of breath-sounds, tubular breathing, and occasional râles. But generally these signs were slight and obscure. There was only a little diarrhœa occasionally, and never any vomiting. The following extracts from the clinical notes put down chronologically give some indication of the conditions found:—"Nearly all the signs have disappeared. . . . Slight diminution of breath-sounds all over the left side, especially at the base. . . . No dulness at all, only a few râles on the left side. . . . Lung resonant, râles both sides. . . . Lung signs quite clear, but child more cachectic. . . . Left chest appears to be a little smaller than the right; the breath-sounds are weak at the base." The case was looked upon as being either simple marasmus with secondary pulmonary collapse or broncho-pneumonia, or tuberculosis with old pleurisy.

CASE 3.—H. L—, was a male patient of 2½ years who was thought to be suffering from pertussis and marasmus with secondary bronchitis, but the autopsy showed that he had double old empyemata at the posterior bases. Besides this, a pericardium recently adherent, except where a small pocket over the right auricle was filled with inspissated pus, was present, and recently adherent pleuræ. He was a pale and wasted infant, with a temperature varying between 97° and 102°, a pulse of 162, and respirations usually over 60 per minute. He had been ailing for nearly two months previously to admission; wasting and paroxysmal cough had come on gradually after measles. The only abnormal physical signs noticed in the chest were those of bronchitis. The paroxysmal cough was accompanied with a suggestion of whoop. He was an in-patient in the hospital for sixteen days altogether. At the end his decline was very rapid.

CASE 4.—C. S.—, a male child of 18 months, is one of the few cases seen in which a definite date could be fixed to the onset of the illness. He had pneumonia a month before admission to the hospital, and although apparently recovering from it fairly soon, he had never been really well since that illness. He had had some cough ever since the onset of the pneumonia, and for a fortnight before admission had been wasting, peevish, and without appetite. There was never any diarrhoea or vomiting. He was not much emaciated, but there was considerable pallor. He had well-marked signs of consolidation all over the left side of the chest; but at the extreme base it was noticed that the breath-sounds were slightly diminished in loudness, and, in addition, the vocal resonance was thought to be a little impaired. An empyema in this region was suspected, consequently exploratory puncture was performed, but with negative result. Subsequent events showed that in all probability one puncture had entered the purulent cavity, but had failed to draw off any pus, because of the inspissated character of the purulent material. The infant was in the hospital for a little under a fortnight. Except on two occasions, once on admission when the temperature was  $105^{\circ}$ , and once later when it was  $100^{\circ}$ , the temperature was never above  $99^{\circ}$ . Persistent rapidity of pulse was a well-marked feature. The day before death the heart-sounds were noticed to be distant, and there was a pad of œdema over the left flank. The autopsy showed that the whole of the left lung was in a state of collapse, there was an old sacculated collection of pus at the left posterior base, and a purulent pericarditis which looked as if it had been present almost as long as the empyema.

CASE 5.—R. W.—, male, aged 3 years, was admitted to the hospital in a very critical condition. According to the history he had had two attacks of "inflammation of the lungs" during his second year, and measles two and a half months before admission. Since the measles he had been

losing flesh, although eating well, and three weeks before being admitted to the hospital he had suffered from profuse and offensive diarrhoea. When admitted he was very ill and fretful, pale, and wasted. The chief symptoms pointed to an abdominal lesion, and he was thought to have tuberculous peritonitis. It was noticed that the heart-sounds at the base were not very clear, but the pulmonary signs were so indefinite, and the chief attention being attracted to the abdomen, the lungs and pleuræ were thought to be free from disease. The temperature was irregular. The patient died in four days, and at the autopsy an empyema was found, with purulent peritonitis and pericarditis. The empyema is described by the pathologist as follows :—"There is a collection of cheesy pus on the left side ; it is an old empyema cut off by adhesions, between the level of the sixth rib and the diaphragm."

CASE 6.—G. C—, aged 23 months, a male, was a patient who had a small sacculated empyema at the right posterior base. His chest was never explored, because, although it was noticed when he was first seen that some impairment of resonance at the right base was present, this was never considered sufficiently definite to justify exploration ; and later he developed so many secondary pulmonary complications that these were considered enough in themselves to account for his symptoms. At the autopsy, besides the old empyema, the following conditions were found :—Collapse of lung at the right base, general bronchitis with slight broncho-pneumonia, and recent pleurisy with some effusion on the left side.

In conclusion I beg to acknowledge with gratitude the helpful criticism I have received from Dr. Rolleston in the compilation of this paper, and to thank the physicians of St. George's Hospital for their kind permission to make use of the cases under their care.

## DISCUSSION.

Dr. DE HAVILLAND HALL considered that the paper was of service in drawing attention to a group of cases, instances of which were frequently overlooked. He himself, when in charge of the children's ward in Westminster Hospital, was always in fear lest he should miss a small empyema. He wished to endorse the opinion expressed in the paper that it was only by repeated examination of the chest that this was to be avoided. In regard to the interlobular form of empyema in childhood, the diagnosis, he thought, would usually be impracticable. This form was hardly saccular, but really a thin layer of pus between the lobes of the lung. The diagnosis in basic cases was easier, but except for the use of exploratory puncture it would often be hardly possible, the signs were so indefinite. He agreed as to the risk of resecting a rib in a debilitated child, and quoted a case with a fatal termination, apparently caused by the operation. However, in cases which were going downhill, with a reasonable supposition of pus, more than an exploratory puncture should be undertaken. The confusion of the diagnosis arising from an initial pneumonia was emphasised, the dulness being attributed to a thickened pleura. Repeated puncture should be employed; it gave really very little discomfort. Reference to the use of the X rays in differential diagnosis was made; in one case alluded to they allowed of the recognition of a subdiaphragmatic abscess. In the cases described in the paper had the urine been examined for albumose?

Dr. HERBERT FRENCH asked how, in the primary cases, the micro-organisms got into the pleural cavity. Apart from the physical signs leucocytosis was a valuable differential sign, especially in distinguishing cases of empyema from those of tuberculosis. Had Dr. Pearson made an examination of the blood in his cases?

Dr. G. A. SUTHERLAND alluded to overlooked cases in his own experience. The term "latent" seemed to include more than one class of case—those in which, at any rate, suggestive symptoms existed, the others in which the condition was not suspected until it was discovered at the necropsy. In the former the exact position of the pus was the doubtful point. A sign in practice sometimes useful was to rest the child on the sound side, when, after full inflation, an area of dulness might be detected. He deprecated the making of numerous punctures, and thought that if two or three punctures were made ineffectually no more should be done. He considered that resection of a rib was a proper measure of treatment when the exploring needle

failed to find the pus, as thereby every part of the lung could be explored. An operation on a localised abscess could be completed at one time, and recovery might be expected.

Dr. F. E. BATTEN considered that from resection of a rib it was not possible to investigate the whole condition of the lung on account of the thickened pleura, and little was gained unless the cavity of the empyema was opened. He doubted if the presence or absence of leucocytosis was of much diagnostic value, and referred to a case in which there was no leucocytosis, and yet an empyema was found at the necropsy. When the pus was between the middle and lower lobes on the right side he believed a diagnosis of interlobular abscess was possible. The form of organism present was not always the pneumococcus; in some it was the streptococcus when the pus was thin, not cheesy. In regard to diagnosis, caseous pneumonia of the whole of one lung from ulceration of a tuberculous gland into a bronchus was apt to mislead. In his experience the onset was commonly acute, unlike the onset in the cases of tuberculosis; he attached considerable diagnostic importance to this. Had a bacteriological examination been made in all of the cases mentioned in the paper, and, if so, had any other organism than the pneumococcus been found?

Dr. HECTOR W. G. MACKENZIE thought the majority of cases of empyema in infants were of a latent character. A history of acute onset, with symptoms like those of acute pneumonia, could sometimes be obtained, and this was a valuable help in the diagnosis. In regard to treatment, exploratory puncture was occasionally very unsatisfactory; if there were good reasons to suspect empyema he would have resection of rib performed at once. He described two cases in which exploratory puncture had failed to find pus. In one of these, which was a case of interlobar empyema, the pus was evacuated, although with difficulty, after resection.

Dr. NEWTON PITT alluded to the cases in which the temperature remained normal throughout the whole course of the disease. Two such were described. The slight cedema of the skin over an empyema was of help in diagnosis, as shown on pinching up the skin, by a difference of thickness on the affected side. These cases are often overlooked because of the preconceived idea that the case is one of pneumonia. Another error was the idea that very loud breathing could not occur over an empyema. There was clinical evidence that recovery might occur by absorption of the fluid in cases due to pneumococci, but this did not apply to the streptococcal cases. The value of leucocytosis was great in facilitating the diagnosis of pus in the pleural cavity. He referred to two cases in which it was present, but the pus was only found after repeated explorations. The ordinary needles are far too small for the successful exploration of

pneumococcal empyemata; pus might be extracted with a large needle after a small one had given negative results.

Dr. VERE PEARSON, in reply, acknowledged the value of leucocytosis in diagnosis. He had, however, met with a case in which there had been leucocytosis, and pus was found, but it proved to be a case of caseating tuberculosis with secondary pneumococcus infection. Of the use of the X rays he had had experience, with great satisfaction in such cases. In regard to unresolved pneumonia, the diagnosis from empyema was often very difficult—time and repeated examination would clear up the diagnosis. He had never examined for albumose. He had almost always found in his cases a history of a deliberate onset. Some of the empyemata were certainly due to streptococcus infection, but the majority were, he thought, pneumococcic.



A STATISTICAL INQUIRY  
INTO THE  
PROGNOSIS AND CURABILITY OF EPILEPSY  
BASED UPON THE RESULTS OF TREATMENT

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(A) *Introduction.*

MUCH attention has been given from classical times onwards to the prognosis of epilepsy. It would, however, serve no useful purpose to refer to the numerous authorities on this disease, or even to briefly state their conclusions. An exception ought, however, to be made in the case of Hippocrates, in whose writings will be found much that is of value even at the present time. For example, when describing the "Sacred Disease" he wrote:<sup>1</sup> "If it attacks little children the greater number die. . . . If youths and young adults, recovery may take place, but there is danger of its becoming habitual, and even increas-

<sup>1</sup> Sydenham Society's translation, vol. ii, p. 850 *et seq.*

ing if not treated by suitable remedies. Such also is the case when it attacks children. . . . When it attacks people of advanced years it often proves fatal. . . . When a person has passed the twentieth year of his life the disease is not apt to seize him, unless it has become habitual from childhood. . . . When the disease has prevailed for a length of time it is no longer curable."

It would appear, however, as if the ancient Greek and Roman physicians took a more generally favourable view of the disease than has been the custom in more recent times.

The essentially gloomy view of the prognosis which has attended the study and treatment of the malady up to the present time may be largely ascribed to the writings of the French physicians in the earlier decades of the last century. Gloomy indeed is the general impression obtained from the writings of Maisonneuve (1803), Pinel (1818), Esquirol (1838), Valleix (1851), and others. More cheerful are the results recorded by such writers as Herpin (1852) and Trousseau (1861) in France, and Russell Reynolds (1861) in this country, who corroborate the opinion expressed by one of the earliest of the French authors, Tissot (1778-80), who almost alone in the eighteenth century stated that he had cured a great number of epileptics, and believed that much could be done towards the arrest of the malady.

A few statistics on the subject may be given here with a view of showing the variability existing between the results obtained by treatment at different periods. In the pre-bromide days it is interesting to recall the high percentage of so-called cures which have been recorded; thus Hufeland<sup>1</sup> stated that a cure was effected in 5 per cent. of his cases. Russell Reynolds<sup>2</sup> noted that 10 per cent. of his cases were cured; Trousseau obtained 20 cures out of 150 cases, or 13 per cent.; and Herpin<sup>3</sup> was perhaps

<sup>1</sup> Hufeland, 'Manuel de Méd.,' 1841.

<sup>2</sup> R. Reynolds, 'Epilepsy,' 1861.

<sup>3</sup> Herpin, 'Du Pronostic,' 1852.

justified in his sanguine belief when he recorded 19 cures out of 38 cases, or 50 per cent. These are the results recorded by physicians who used remedies (such as oxide of zinc and nitrate of silver) which have long ago passed out of present-day practice.

The almost universal administration of bromides, since their introduction in 1857 in the treatment of this disease, has in no way affected the variability in the results obtained. To mention a few instances :

Nothnagel gives from 4 to 5 per cent. of cures.

Læhr „ 6 per cent. of cures.

Ackermann „ 7·6 „ „

Dana<sup>1</sup> „ from 5 to 10 per cent. of cures.

Wildermuth „ 8·5 per cent. of cures.

Habermaas<sup>2</sup> „ 10·3 „ „

Alt „ 12·5 „ „

It must be evident that some explanation ought to be forthcoming as to the difference existing between the statistics of recent authors upon the results obtained before and since the introduction of the bromide treatment. First, some proportion of the existing difference is accounted for by the greater precision exercised in diagnosis, the later authors excluding from their statistics all cases of symptomatic epilepsy, or epilepsy arising from organic cerebral or meningeal disease, and of hystero-epilepsy. It is within the knowledge of most neurologists that the prognosis of symptomatic epilepsy is more favourable than that of true epilepsy, but an obvious proof of this fact may be found on perusal of Reynolds'<sup>3</sup> figures, which show 10 per cent. of cures in the idiopathic disease, and 43 per cent. in that due to organic cerebral disorders. Secondly, much of the discrepancy existing in statistics depends upon the definition of a cure, the interpretation differing widely in nearly every writer's statements.

<sup>1</sup> Dana, 'Text-book,' 1898.

<sup>2</sup> Habermaas, 'Allg. Zeitsch. f. Psych.,' vol. lviii, p. 243, from which the other references are taken.

<sup>3</sup> Russell Reynolds, 'Epilepsy,' London, 1861.

Reynolds regarded only those cases as cured in which there had been perfect restoration to health during a period of at least four, or at most eight, years after cessation of the seizures; but many authors fail to state in their writings what is their definition of cure, or recovery, from epilepsy, and in the majority of instances so-called cures are merely long remissions occurring spontaneously or induced by suitable medicinal remedies.

It would seem to be obvious from Voison's statement that Herpin's were really cases of permanent cure, for he observed many of these patients ten years after Herpin's death and found them free from fits.<sup>1</sup>

(B) *The Statistics.*

It has been thought advisable that the records of the Out-patient Department of the National Hospital for the Paralysed and Epileptic, which contain an enormous amount of valuable information in this connection, might be advantageously studied with a view to collecting and analysing the experience of many years in the treatment of this disease, under the influence of the bromides and the more recent medicinal remedies. I am therefore greatly indebted to my colleagues in the Out-patient Department of the Hospital for permission to refer to their case records, and to add them to those which have been under my own observation. A few cases have also been obtained from private sources.

I have reserved for special consideration in a further communication the cases which have come under care and treatment at the Colony for Epileptics, Chalfont St. Peter, amounting to about two hundred in number. The reason for this separation is obvious, in that those cases which eventually find their way into this and similar institutions have previously to their admission been under various forms of medicinal treatment, and from which they have received

<sup>1</sup> Mentioned by Nothnagel, 'Ziemssen's Encycl.,' vol. xiv, 1878.

no permanent benefit, and have become, in the majority of instances, confirmed epileptics. The hospital cases, on the other hand, are mainly early examples of the disease, with little or no mental impairment, and are perfectly capable of continuing their schooling or attending to their several occupations.

In analysing the cases certain guiding principles were laid down, and the following eliminations were made :

1. All cases which had not been under constant observation and treatment for a period of at least two years.
2. All cases which showed any co-existing complication, such as hemiplegia, albuminuria, or gross cerebral lesion.
3. All cases of pronounced idiocy or dementia.

By observing these restrictions, cases of so-called idiopathic epilepsy were as far as possible obtained, while any transitory amelioration, resulting from medicinal or other treatment, was checked by fixing the minimum period of observation at two years.

In the study of the cases the statistical method has been adopted, and the results have been recorded in percentages, the total number of cases used in the construction of each table being also given. Although many objections may be urged against such a method, it has been deemed to be the best available, while the results, as will be seen later on, show a surprising uniformity when considered from various points of view.

The total number of cases used in the investigation is 366. Of these 355 are from the records of the out-patient department of the Queen Square Hospital, while only eleven are from private sources. By far the larger proportion are out-patient hospital cases, a fact of practical importance when we consider how large a part the ordinary conditions of life, such as diet, habits, and general environment, play in modifying a disease like epilepsy.

The cases have been subdivided into three groups according as they have responded, successfully or unsuccessfully, to treatment.

TABLE A gives the total number of cases and the general result of treatment.

Cases of arrest . . .	86	Observed over nine years . .	38 cases.
Cases showing improve- ment . . .	105	" "	43 "
Confirmed cases . . .	175	" "	66 "
	<hr/> 366		<hr/> 147

The term *arrest* has been used at the outset advisedly in preference to *cure*, owing to the uncertainty in defining the latter term. No case has been regarded as arrested which has not been free from fits for a period of at least two years. The cases classified as *improved* are those which have responded more or less satisfactorily to treatment. Under this heading are also included those cases in which a remission, sometimes for a number of years, has occurred, but in which a relapse has eventually taken place. *Confirmed* cases are those which have shown a steady tendency, though not necessarily a progressive one, to mental deterioration, without any material lessening either in the frequency or the severity of the seizures.

In the second column of the table is given the number of cases which were observed for a period of nine years or more. The importance of this column will be seen in a subsequent part of the paper.

Of the total of 366 cases no less than 86 showed an arrest of the seizures over periods varying from 2½ to 25 years. The majority of these continued the bromide treatment during the whole period of arrest, so that, with few exceptions, the amelioration cannot be described as other than arrest during the administration of the bromides. In all cases, owing to the patient passing from under observation after a number of years, no further record has been obtainable. It is, however, no uncommon thing to meet with a past history of this disease in adults and elderly people suffering from symptoms of nervous debility and neurasthenia, who give an account of having

many years before been subject to attacks of an epileptic nature, and of which they have been cured. Two instances of this may be given :

CASE 1.—A man, when 18 years of age, had an epileptic fit. This was followed by two more attacks during the next eighteen months. He was kept upon bromide treatment for four years, and as there was no recurrence of the fits the medicine was stopped. Fifteen years later, when aged 35 years, he came under treatment for general neurasthenic symptoms, having had no relapse of the epileptic attacks.

CASE 2.—An unmarried woman had a number of epileptic fits between the ages of 28 and 32 years. She was under treatment by bromides for one year only. Twenty-two years later, when 54 years of age, she came under observation for headache and nervousness, having had no further attacks of epilepsy since she was 32. During this period she had no treatment of any kind.

The subjoined table (B) gives the total number of cases in which arrest took place and the length of time during which no fits were noticed, the bromides being all the while administered, except where stated to the contrary.

TABLE B *gives the number of cases in which arrest took place, and their duration.*

11 cases of arrest of from 2 to 3 years' duration.					
18	"	"	"	3 to 4	" "
10	"	"	"	4 to 5	" "
11	"	"	"	5 to 6	" "
5	"	"	"	6 to 7	" "
8	"	"	"	7 to 8	" "
8	"	"	"	8 to 9	" "
4	"	"	"	9 to 10	" "
5	"	"	"	10 to 11	" "
2	"	"	"	11	" "
2	"	"	"	15	" " (without bromides).
1	"	"	"	22	" "
1	"	"	"	25	" "

As it is highly desirable to ascertain how far epilepsy is a disease which may be arrested, improved, or become confirmed, it is proposed to study the cases which have been collected, and the influence of treatment upon them under various headings, so as to define, as far as possible, the specific factors upon which a prognosis may be based. The method adopted in this paper is one of percentages, the total number of cases in the several tables showing slight variations, according as the information supplied by the notes threw light upon the points specially under investigation.

The prognostic bearing and value of the following influences will therefore receive separate consideration.

(c) *Conditions influencing Prognosis.*

The prognosis of epilepsy, and the conditions which influence it, will be discussed in detail. It is proposed to deal with this subject under the following headings :

1. The influence of an hereditary disposition.
2. The influence of age at the onset of the disease.
3. The duration of the disease.
4. The frequency of the seizures.
5. The character and time of the seizures.
6. The influence of marriage.
7. The influence of pregnancy, parturition, and the puerperium.
8. The influence of sex.
9. The influence of the catamenia.
10. The influence of accidental factors.

After the above have received consideration on the basis of the collected cases, attention will be directed to certain types of epilepsy which have an influence on the prognosis, and also to the important subject of long remissions in epilepsy and their bearing upon the cure of the disease.



### 1. *The Influence of an Hereditary Disposition.*

For the purposes of this investigation a family predisposition to epilepsy only, *i. e.* a similar heredity, has been noted. The influence of the neuroses, such as chorea, migraine, alcoholism, and insanity, has been for the present purpose omitted from the statistics.

TABLE C *gives the total number of cases in which this point was investigated.*

	Arrests.	Improved.	Confirmed.	Total.
Epilepsy on mother's side .	16	16	18	50
Epilepsy on father's side .	12	11	14	37
No known heredity to epilepsy	42	59	24	125
No note of heredity . .	12	19	119	150
				<hr/> 362

In the above table (C) a total of 362 cases has been analysed ; of these 150 may be eliminated, as there was no note either for or against any hereditary predisposition. Of the remainder there was a clear family history of epilepsy in 87, while the existence of this disease in the family was unknown to the patient or the relatives in 125. The malady was slightly more common upon the mother's than upon the father's side.

TABLE D *gives the percentage of hereditary and non-hereditary cases.*

	Arrests. Per cent.	Improved. Per cent.	Confirmed. Per cent.	Total Cases.
With hereditary history .	32·0	31·0	36·0	87
Without hereditary history .	33·6	47·2	19·2	125
				<hr/> 212

From this table (D) it is seen that there is practically the same percentage of arrests in those with, as in those without an hereditary history ; the latter, moreover, showing a greater percentage of improved cases and a decidedly smaller percentage of cases which eventually became confirmed.

The general prognostic conclusions which may be drawn from these cases are—

(a) That there is as great a chance of arrest of epileptic fits in those who have, as in those who have not a known family history of epilepsy.

(b) In those who have an hereditary history the chances as to whether the fits become arrested, improved, or confirmed are in any given case about equal.

(c) That as regards general improvement, more is to be expected in those who have no hereditary disposition, while a considerably smaller percentage of confirmed epileptics is to be found amongst those who have no family predisposition to the disease.

## 2. *The Influence of Age at the Onset of the Disease.*

In the subjoined table (E) the percentages are given in the first three columns, the total numbers being stated in the last.

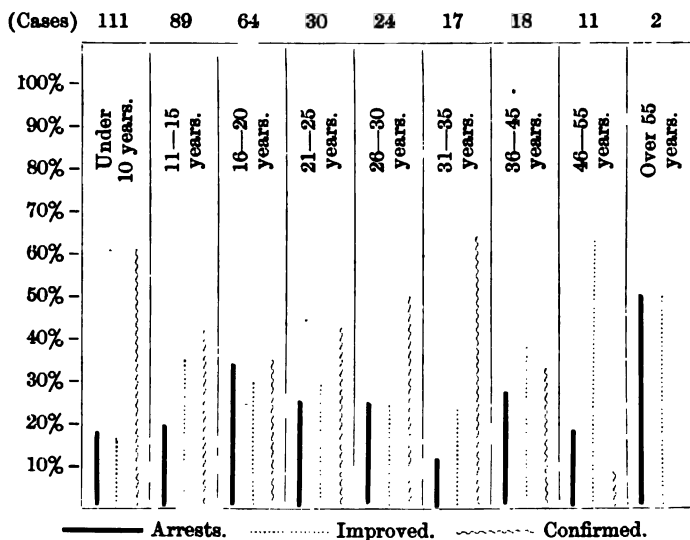
TABLE E shows the age percentage at the onset of the fits.

Age at onset.	Arrests. Per cent.	Improved. Per cent.	Confirmed. Per cent.	Total Cases.
Under 10 years . . .	19·8	18·0	62·0	111
11 to 15 „ . . .	20·0	35·9	43·8	89
16 to 20 „ . . .	34·3	29·6	35·9	64
21 to 25 „ . . .	26·6	30·0	43·0	30
26 to 30 „ . . .	25·0	25·0	50·0	24
31 to 35 „ . . .	11·7	23·5	64·7	17
36 to 45 „ . . .	27·7	38·8	33·3	18
46 to 55 „ . . .	18·1	63·6	9·0	11
Over 55 „ . . .	50·0	50·0	—	2
				<hr/> 366

The accompanying chart (Chart I) is of especial value, as it shows that the age at the onset of the disease is particularly important in considering the prognosis. In order to facilitate the comprehension of the figures in the above table (E), the following graphic method has been adopted :

CHART I.

Total number of cases, 366.



The main conclusions to be derived from a perusal of the above may be stated as follows:

(a) Epilepsy commencing under 10 years of age is least favourable as regards arrest or improvement, and most favourable for the production of confirmed cases.

(b) Those cases in which the onset of the disease is between 16 and 20 years of age show the greatest percentage of arrests and the lowest percentage of confirmed cases. From this quinquennial period onwards to that of 31 to 35 there is a steady diminution in the percentage of arrests, and a progressive increase in the percentage of confirmed cases.

The chief point of practical importance to be deduced from these figures, if put in general terms, is that epilepsy arising during puberty is essentially a tractable disorder, while that of adolescence is resistance to treatment. These facts and figures confirm in a striking manner the opinion of Hippocrates, who wrote, "Epilepsy which commences

about puberty is susceptible to cure, while that which comes on after 25 years of age as a rule only terminates with the patient."<sup>1</sup>

(c) From that arising during the quinquennial period 31 to 35 years (which provides the least tractable form of epilepsy, except perhaps that commencing under 10 years of age), there is a steady diminution in the number of cases which become confirmed, so much so that of those cases which arose during the decennial period 46 to 55 years, only 9 per cent. became confirmed epileptics.

(d) Epilepsy arising over 55 years of age, to which the name of senile epilepsy has been applied by some writers, is essentially a tractable disorder.

### 3. *The Influence of the Duration of the Disease.*

In the two following tables the duration of the malady is considered, the percentage frequency being given in the first three columns, the total number of cases in the last.

The term "duration" signifies the course of the disease from its commencement until the patient came under regular observation and treatment at the hospital, from which time there dated either arrest of the fits, improvement, or a steady downward deterioration.

TABLE F *gives the duration percentage of the disease up to the commencement of treatment, and the general result of treatment.*

Duration.	Arrests. Per cent.	Improved. Per cent.	Confirmed. Per cent.	Total Cases.
10 years and under . . .	23·5	32·3	44·1	272
11 to 20 years . . .	25·8	19·3	54·8	62
21 to 30 „ . . .	12·5	20·8	66·6	24
31 to 40 „ . . .	20·0	—	80·0	5
Over 40 „ . . .	50·0	—	50·0	2
				365

<sup>1</sup> 'Aphorisms,' Section 5, No. vii. The aphorism is rendered in the Sydenham Society's translation, vol. ii, p. 738, as follows:—"Those cases of epilepsy which come on before puberty may undergo a change, but those which come on after 25 years of age for the most part terminate in death."

The above shows, by division into decennial periods, that there is as great a percentage of arrests when the disease has lasted from 10 to 20 years as from 1 to 10 years, but that under 10 years the percentage of improved cases is greater, and there is less tendency for the disease to become confirmed. But as ten years is a considerably prolonged period, and as the majority of epileptics come under observation and treatment before so long a time has elapsed, it is important to ascertain the percentage frequency for periods short of ten years, and this has been done in the following table:

TABLE G *gives the percentage frequency in four unequal periods under 10 years of age.*

Duration.	Arrests. Per cent.	Improved. Per cent.	Confirmed. Per cent.	Total Cases.
Under 1 year . . . .	29.1	38.8	31.9	72
1 to 3 years . . . .	29.8	32.1	39.0	87
3 to 5 „ . . . .	20.4	29.5	50.0	44
5 to 10 „ . . . .	11.5	27.8	60.8	69
				<hr/> 272

Some general conclusions may be drawn from a perusal of these tables, as well as from a study of the subjoined chart (Chart II), which gives in a graphic form the percentage results already detailed.

(a) Speaking in general terms, the earlier a case is brought under systematic treatment the more hopeful the prognosis and the greater the probability of improvement.

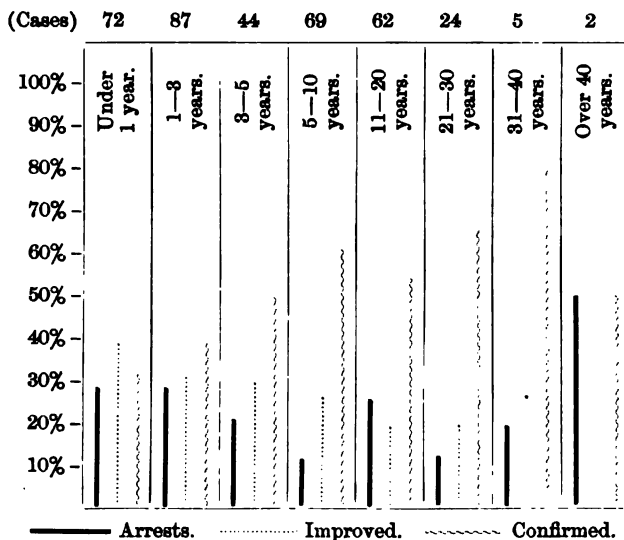
(b) That there is a greater prospect of arrest or improvement during the first five than during the second five years of the disease.

(c) Arrest of the fits, however, may take place in cases even after a duration of from 20 to 30 years. After 30 years arrest is possible, but the fewness of the cases hardly allows of any definite conclusions.

(d) There is a progressive tendency for epilepsy to become confirmed the longer the disease lasts without definite treatment.

## CHART II.

Total number of cases, 365.



A comparison may now usefully be made between Tables E and G, which show respectively the age and duration percentages, and the following table (H), which shows the age-periods at which arrest most commonly took place.

TABLE H shows the age-periods at which arrest took place in eighty-six cases.

Under 10 years of age . . . . .	6 cases, or 6·9 per cent.
From 11 to 15 years of age . . . . .	8 " 9·2 "
" 16 to 20 " " . . . . .	15 " 17·4 "
" 21 to 25 " " . . . . .	17 " 19·7 "
" 26 to 30 " " . . . . .	9 " 10·4 "
" 31 to 35 " " . . . . .	8 " 9·2 "
" 36 to 40 " " . . . . .	7 " 8 "
" 41 to 45 " " . . . . .	7 " 8 "
" 46 to 50 " " . . . . .	4 " 4·6 "
Over 50 years . . . . .	4 " 4·6 "
A doubtful case . . . . .	1

From these tables it is obvious that the decade 16 to 25 presents the greatest number of arrests ; in other words, more arrests are likely to take place during the latter part of that decade, in the earlier part of which the onset of true epilepsy is most common,—that is to say, the quinquennial period 16 to 20, in which the disease most usually declares itself, is succeeded by the quinquennial period 21 to 25, in which arrest is most frequent. This observation would corroborate the interpretation put upon the figures given in Tables F and G, from which it is clear that epileptic fits are more prone to arrest during the first three or five years following their onset.

#### 4. *The Frequency of the Seizures.*

The relative or average frequency of the attacks has an important bearing upon the prognostic outlook, as will be readily seen from the following table :

TABLE J gives the percentage frequency of the attacks.

Frequency.	Arrests. Per cent.	Improved. Per cent.	Confirmed. Per cent.	Total Cases.
Daily (1 or more) . . . .	—	42·5	57·5	40
Weekly (1 or 2) . . . .	12·5	23·9	63·5	96
Monthly (1 or 2) . . . .	22·9	31·2	45·8	96
Quarterly (1 or 2) . . . .	36·9	24·6	38·4	65
Yearly (1 or 2) . . . .	42·1	47·3	10·5	19
				<hr/> 316

The general conclusion may be drawn that the longer the interval between the attacks the greater the prospect of arrest or improvement. Very infrequent attacks are eminently favourable. Attacks which occur every three or four months, or once or twice a year, are—within certain limits, and when considered in association with the points already mentioned in previous paragraphs—of more satisfactory prognostic importance than those which may be counted by the month, the week, or the day. The greatest percentage of confirmed cases, and the smallest percentage

of arrested cases, are seen from the above table to occur in those epileptics who are subject to daily and weekly attacks; and the converse also holds good, in that the smallest percentage of confirmed, and the highest of arrested cases, are found amongst those epileptics whose fits occur so infrequently as once or twice a year.

### 5. *The Character and Time of the Seizures.*

The kind of attack to some extent modifies the prognosis. It is matter of common knowledge that the major attacks are more readily influenced by drugs than the minor seizures. Owing to the incompleteness of the note in describing the exact character of the fits, it has been found impossible to construct a table of any real value, but so far as information has been supplied it is clear that the greatest percentage of arrests is to be found in cases of grand mal (49 per cent. out of a total of 96 cases); then follow the cases of combined grand and petit mal (35 per cent. out of a total of 56 cases); and lastly, petit mal occurring alone (26 per cent. out of a total of 15 cases).

So also with regard to the time-incidence of the seizures. Those occurring by day only—including in this the very common early morning seizure—give a greater percentage of arrests (51·9 per cent. out of a total of 52 cases) than those occurring only during sleep (34 per cent. out of a total of 35 cases). Combined day and night attacks give also an arrest percentage of 34 per cent. out of a total of 35 cases.

### 6. *The Influence of Marriage.*

There would appear to be no real foundation for the popular belief that marriage predisposes towards cure, or even amelioration, of epileptic seizures. On the contrary, the consequences of matrimony tend to the production of circumstances distinctly unfavourable to the arrest, or alleviation, of the disease.



Of thirteen cases in which the disease was specially observed in its relation to marriage (all being women), five stated that they observed no change at all either in the frequency or the character of their fits; five appear to have slightly improved, in one of whom the improvement was only temporary; of the remaining three, one had her first seizure on the night of her marriage, another developed epilepsy seven months after marriage, while the third case seems to have been distinctly affected for the worse by marriage.

These observations are in general harmony with what has been stated by other writers—namely, that there is no constancy in the influence of marriage upon the seizures.<sup>1</sup>

The influence of marriage upon the transmission of the disease is a subject which scarcely comes within the scope of this paper; but some facts bearing upon it are incidentally mentioned and will be here briefly stated.

CASE 3.—A married woman, suffering from epilepsy, whose maternal grandfather had fits, bore six children, all of whom died of convulsions in infancy.

CASE 4.—Two epileptics, husband and wife, had six children. Three daughters and a son were well and without fits. Two other daughters, aged 16 and 18 years, developed fits when they were respectively 13 and 14 years old.

CASE 5.—A married epileptic woman, without any known heredity to the disease, had ten children, the eldest of whom was 37 and the youngest 20 years old. None of them had convulsions or fits.

CASE 6.—A married epileptic woman, whose two brothers also had fits, had a daughter who was also an epileptic.

<sup>1</sup> On this point see some statistics collected by A. Hughes Bennett, 'Brit. Med. Journ.,' March, 1879.

CASE 7.—An epileptic man, without any known heredity, had ten children, the youngest of whom was 36 years of age. None of them had fits.

CASE 8.—An epileptic man without heredity, who had fits from 16 to 69 years of age, had two children, neither of whom had fits.

CASE 9.—A married epileptic woman had two children without fits, but both of them had an attack of chorea.

The above form only a small number of cases, but one fact stands out—namely, that of the three parents in whose family there was no known history of epilepsy, epileptic fits had not appeared in the children; that in the two cases in which the disease was obviously hereditary, fits or convulsions were present in the offspring; that in the case in which both parents were epileptic, two out of six children developed epilepsy.

#### *7. The Influence of Pregnancy, Parturition, and the Puerperium.*

The influence of pregnancy has been noted in twenty cases. Of these, nine were free from seizures during this period, one patient stating that her longest free intervals occurred when she was in this condition. Of the remainder, seven were invariably worse when pregnant, two had fits only at or about the time of quickening, and one never observed any difference either in the frequency or character of the fits. In another case, in which the fits were arrested by bromides for a long time, an intercurrent pregnancy and subsequent puerperium intervened without any symptoms of epileptic seizures.

It may therefore be concluded that gestation has little, if any, influence upon the disease. At the best there may only be a temporary respite; but pregnancy is the forerunner of the puerperium, a period which is especially

prone to epileptic attacks. Of nineteen cases in which this state was noted, all gave a history of one or more severe attacks within a short period, usually a few days after the birth of the child. In two of the cases the onset of the disease was observed after the birth of the first baby, and in one after the birth of the fourth child.

Lactation would seem in some cases to be peculiarly favourable for the occurrence of fits. In one case the fits only came on during the period of suckling, and this happened after three successive pregnancies. On weaning the fits disappeared. In a second case the first fit arose while nursing the first baby four months after confinement.

From the above facts it would appear as if there were three periods when epileptic fits were prone to develop—at quickening, during the first few days of the puerperium, and during lactation.

### 8. *The Influence of Sex.*

Sex plays little part in the prognosis of epilepsy. The following table will show the percentage of arrested, improved, and confirmed cases in this relation. From this it is seen that rather more males show arrest of the seizures, but at the same time this sex gives a greater percentage of confirmed cases.

TABLE K *shows the sex percentage of arrested, improved, and confirmed cases.*

	Arrests. Per cent.	Improved. Per cent.	Confirmed. Per cent.	Total Cases.
Males . . . .	26	22	51	179
Females . . . .	20	34	44	187
				<hr/> 366

These results are in harmony with those of several previous observers (Reynolds, Gowers, and others), but are in opposition to the statement of Herpin.

### 9. *The Influence of the Catamenia.*

Menstruation would appear to exert little influence upon the prognosis of epilepsy. The popular belief that the satisfactory and regular establishment of this function will arrest or ameliorate the disease has no scientific basis. The onset of epileptic fits during puberty is not uncommonly accompanied by irregularity in the menstrual periods; but it is rare to find any amelioration in the frequency or severity of the attacks when the period becomes regularly established. It will be seen that amenorrhœa induced physiologically by pregnancy may or may not have any beneficial effect. There were some cases also in which the fits became arrested at or about the climacteric period, but the evidence is too small to state definitely that this is an epoch at which spontaneous arrest may be expected. A reference to Table H will show that 8 per cent. of the cases were arrested between the ages of 41 and 45, but only three of these were women. There was one patient, however, who seemed to lose her fits when she was subject to amenorrhœa, from which she occasionally suffered for prolonged periods. During these periods she was invariably free from attacks, which reappeared when the catamenia were established.

### 10. *The Influence of Accidental Factors.*

A few words may be said upon the influence of accidental factors in relation to the production of epileptic fits. In two cases an intercurrent attack of pneumonia was noted. In one, although several seizures occurred during the course of the pulmonary inflammation, a respite from fits was subsequently obtained lasting for several months. In another, during a long spell of freedom from fits an attack of pneumonia brought about a temporary return of the seizures. In another patient an attack of chorea was followed by a year's freedom from fits. In

another an attack of scarlet fever greatly increased the number and severity of the epileptic seizures. In another case a long interval of freedom was broken by the patient receiving a severe blow upon the head. In a case of epilepsy the gradual onset of paralysis agitans made no difference to the pre-existing disease.

As a rule an attack of acute febrile disorder gives a subsequent temporary respite from fits, with the exception of scarlet fever, a fact which has also been noted by Gowers. On the other hand, the *onset* of an acute pneumonia may be accompanied by severe seizures, or by a temporary relapse during a remission from fits. Injuries, such as blows upon the head, aggravate the disease, an observation which is in harmony with what occurs in other chronic nervous disorders.

No prolonged relief from epileptic fits can therefore be predicted after the occurrence of an acute inflammatory disorder.

#### (D) *Types of Epilepsy.*

Even a brief acquaintance with epileptics will show that there is a marked periodicity in the occurrence of the seizures, which is highly characteristic of the disease. The intervals are of varying duration—a day, a week, two weeks, a month, two or three months, a year, or longer. These intervals are, however, not absolutely regular, considerable variability and irregularity being observed on charts specially kept for recording the time-periodicity of epileptic fits. Such, indeed, is the common incidence of attacks; but attention has been directed by Biro<sup>1</sup> to certain types of cases which have apparently some bearing on prognosis.

These types have been called “increasing” or “decreasing,” and some examples will be given to illustrate their characteristics. The types may be described either by the number of fits per month or per year, in

<sup>1</sup> Biro, ‘Deut. Zeitsch. f. Nervenheilk.’ vol. xxiii, 3, p. 40.

increasing or decreasing numbers, or by the number of years or months intervening between the seizures. The following may be taken as illustrative of the types :

(a) *Increasing Type.*

CASE 10.—Fits commenced at 15 years of age. Three fits in the first year (without treatment) ; four in the second year (under bromides) ; nine in the third year (under bromides) ; ten in the fourth year (under bromides). After this the patient ceased attending. It is seen that the fits went on increasing, notwithstanding the continuance of treatment.

CASE 11.—This patient had the first fit when 5 years of age ; second when 11 ; third when 19 ; fourth when 20 ; fifth and sixth when 21. He was then put under bromide treatment, and has had no fits for eight years.

CASE 12.—Fits commenced at 22 years of age. Previous to regular bromide treatment the patient was having about one fit per month. Under bromides she had—one fit in December, 1897 ; interval of two years ; two fits in January, 1900 ; interval of one year ; two fits in 1901 ; three fits in 1902, since which date there has been no further observation.

(b) *Decreasing Type.*

CASE 13.—Fits commenced at 39 years of age. During the first year of bromide treatment, several attacks ; second year, four ; third year, one ; fourth year, two ; fifth year, one ; sixth, seventh, eighth, and ninth years, none.

CASE 14.—Fits commenced at 21 years of age. During the first year of treatment, twelve or more fits ; second year, twelve ; third year, twelve ; fourth year, three ; fifth

year, four; sixth year, two; seventh, eighth, and ninth years, none.

CASE 15.—The patient came under treatment at 19 years of age, having a fit every two or three weeks. During the first year of treatment he had about twelve fits; second year, several; third year, eight; fourth year, four; fifth year, one; sixth year, none.

The two types, as above described, may, upon the other hand, be found blended in the same case; for example, one of increasing character may, as the result of treatment, be changed into the decreasing type, and of this description are the two following cases:

(c) *Blended Increasing and Decreasing Types.*

CASE 16.—First fit occurred at 12 years of age; second after eight years' interval; third after five; fourth after five; fifth after two; batch of three after three. He then came under regular bromide treatment, and had two fits in the next year; three in each of the two following years; five in the next year; one a year later; none in the next three years.

CASE 17.—When aged 25, in 1882, patient had his first fit; 1884, his second; 1884 to 1887, free from attacks; 1887 to 1890, several; 1891, four; 1892, eleven; 1893-4, eight; 1895, six; 1896, three; 1897-8, none; 1899, one very slight; 1900-1901, none.

The above recorded cases, although symbolic of the types referred to, are rarely met in such purity. Their prognostic importance may be briefly stated as follows:

(a) In the increasing type, as shown in Cases 10 and 12, the fits, through a natural inclination to self-perpetuation, go on increasing in spite of treatment. On the other hand, the type may be not unfavourable for arrest, as in Case 11.

(b) The decreasing type is more commonly induced by

treatment, and, if clearly established, has a favourable outlook.

(E) *Long Remissions in Epilepsy.*

It is well known that remissions are a frequent, if not a characteristic feature of this disease. The common remission which takes place during childhood in those whose fits commence in infancy, then cease for a time, and recur at or about the time of puberty, is one of the most remarkable features of this disorder. An interval of several years not infrequently occurs between the first and second attacks, while numerous instances may be cited in which periods of five, ten, or fifteen years have been known to elapse between epileptic seizures. Wharton Sinkler<sup>1</sup> records a remission of twenty-nine years in one of his cases.

An examination of the present series reveals a number of instances in which remissions have been observed, and which have persisted for a number of years, but which have been succeeded by a return of the characteristic seizures.

In the cases in which *arrest* is stated to have occurred, freedom from fits was noted over periods varying from two to twenty-five years (these have not been included in the present table); but in Table L will be found the list of cases which show *remissions* lasting for more than two years, with subsequent relapse.

TABLE L *shows the cases of remission and their duration.*

Remission of from 2 to 3 years observed in 1 case.					
"	"	3 to 4	"	"	2 cases.
"	"	4 to 5	"	"	4 "
"	"	5 to 6	"	"	2 "
"	"	6 to 7	"	"	2 "
"	"	7 to 8	"	"	1 case.
"	"	15	"	"	1 "

<sup>1</sup> Wharton Sinkler, 'Journ. of Nervous and Mental Disease,' 1898, p. 601.



In these cases the remission occurred during bromide administration, and in all of them the fits returned, notwithstanding the continuance of the drug.

As it is from the consideration of such cases that most information may be gleaned with reference to the possibility of a cure of epilepsy, it will be instructive to study some of them with greater detail.

In one case there were two periods of remission, one lasting for three and a half years without any remedies having been given, the other for four years under bromide treatment. The fits eventually recurred with symptoms of automatism and violence. In another an interval of six years of freedom was succeeded by a return of fits in increasing frequency. In a third there were two remissions, one of three years and a second of five years, to be followed by fits occurring about every month. In another an apparent arrest for seven years was broken by two fits during an attack of acute pneumonia. In the patient, remission of whose seizures lasted for fifteen years, the relapse was characterised by the occurrence of *petit mal*.

It should be pointed out that in all the above cases the disease had been fully established for some years, and that the intervals therefore do not correspond to the prolonged periods sometimes found between the first and second fits to which reference has already been made.

Two points especially call for notice in this connection : on the one hand, long remissions may occur under bromide administration, to be followed by a relapse when the drug is omitted ; on the other hand, a remission of long duration may be broken by accidental circumstances, such as a blow on the head, a fall, childbirth, or an acute inflammatory disorder. Hence it is apparent that long periods of arrest, though as a rule indicating a favourable prognosis, are not synonymous with a cure of the disease. The question may therefore now be asked—

(F) *Is there a Cure of Epilepsy?*

This question may in general terms be answered in the affirmative. Two cases (Cases 1 and 2) have been already mentioned in which this occurred, and not a few instances may be gathered from amongst epileptics and neurasthenics, who state that they suffered from fits in earlier years; and if the later histories of epileptics could be traced many more instances might no doubt be added. Although writers are generally agreed as to a cure of epilepsy, there is a less general consensus of opinion as to what is the definition of a cure,—that is to say, after what period of arrest, a “cure” may be said to have taken place.<sup>1</sup> Before attempting to answer this question it is necessary to refer again to a few points to which attention has already been directed. With this object in view, Tables B and L, dealing especially with the cases of arrest and long remission, are blended and reproduced side by side in Table M, which gives the number and duration of the cases of arrest and remission:

TABLE M *gives the cases of arrest and remission, with the duration.*

11 cases of arrest, 1 of remission, from 2 to 3 years' duration.							
18	“	“	2	“	from 3 to 4	“	“
10	“	“	4	“	from 4 to 5	“	“
11	“	“	2	“	from 5 to 6	“	“
5	“	“	2	“	from 6 to 7	“	“
8	“	“	1	“	from 7 to 8	“	“
8	“	“	0	“	from 8 to 9	“	“
4	“	“	0	“	from 9 to 10	“	“
5	“	“	0	“	from 10 to 11	“	“
2	“	“	0	“	of 11	“	“
2	“	“	1	“	of 15	“	“
1 case	“	“	0	“	of 22	“	“
1	“	“	0	“	of 25	“	“
86 Total			13				

<sup>1</sup> Reynolds defined a cure as perfect restoration to health for at least four years, and at most eight years, after arrest of the fits.

The arrest column shows that the greater number of the cases (71 out of a total of 86) were observed over a period of from two to nine years, during which no fits occurred; while of the remission cases, although four showed an arrest from four to five years, in five a relapse occurred up to eight years, after which time only one was found to relapse. When these results are compared in conjunction with those of Wharton Sinkler, who observed only four cases of relapse out of a total of twenty-four after nine years' remission, I have thought it *unsafe to regard as cured any case of epilepsy in which the seizures have been in abeyance for a period of less than nine years* after the disease has become satisfactorily established. This provision is made in order to eliminate all those cases of remission during childhood, which are known to last for seven, eight, or nine years, and also those cases in which long intervals elapse between the first and second, or second and third fits at the commencement of the disease. In order to obtain the percentage of cures in the present series, those cases only have been taken which were under observation for a period of at least nine years. They form a total of 147, of which 15 were arrested for nine or more years (*vide* Table B), *giving a percentage of 10.2 cures.*<sup>1</sup>

Taking the series of cases with long remission recorded in this paper along with those of Sinkler, it is found that a few still remain in which relapse occurred after the nine years' limit, viz. four by Sinkler and one by myself. Therefore, although it may be laid down as a general rule that a cure of epilepsy has been established after an arrest of nine years, the fact must be borne in mind that a very small percentage of cases do relapse after that period.

While discussing the cure of epilepsy, a point of practical importance which should not be overlooked is that

<sup>1</sup> There is a striking harmony between these results and the percentage of cures obtained by Reynolds (10 per cent. with a basis of four to eight years) and Habermaas (10.3 per cent. with a five to ten years' basis).

those who have been cured of their seizures not infrequently show various mental peculiarities, such as impairment of memory, irritability of temper, headache, and a tendency towards neurasthenic symptoms.

(a) *The Curable Cases of Epilepsy.*

Although in the present series of cases there is no definite information as to the mental condition of the patients, clinical experience and observation show that many cases of epilepsy may exist for prolonged periods without any material mental impairment. Such cases would appear to belong to what may be termed a curable type of epilepsy. A special investigation has therefore been made into the duration of the disease before regular treatment was established in the eighty-six cases in which arrest took place. From this it is seen that of forty-four cases in which arrest took place during the first year of treatment, the disease had been in existence during periods varying from one to thirty-five years, with an average duration of seven years.

This investigation also brought forward a point of great importance—namely, that if any given case of epilepsy is capable of amelioration by treatment, a satisfactory response will be shortly apparent, as the following table shows :

TABLE N *shows the influence of bromide treatment upon 86 cases of arrested epilepsy.*

Arrest under 1 year's treatment	.	.	.	44 cases, or 51.7 per cent.
„ „ 2 years'	„	.	.	9 „ or 10.5 „
„ „ 3 „	„	.	.	6 „ or 7.0 „
„ „ 4 „	„	.	.	4 „ or 4.7 „
„ „ 5 „	„	.	.	3 „ or 3.5 „
„ „ 6 „	„	.	.	2 „ or 2.3 „
„ over 6 „	„	(7—22 years)	17 „ or 20.0 „	
An uncertain case	.	.	.	1 case.

From this table it is obvious that over 50 per cent. of the cases in which arrest took place yielded to treatment within the first year of regular bromide administration.

#### SUMMARY AND CONCLUSIONS.

1. A total of 366 cases, chiefly derived from the Out-patient records of the National Hospital for the Paralysed and Epileptic, has been used for the investigation.

2. Only cases of genuine idiopathic epilepsy, which had been under constant observation and treatment for a period of at least two years, have been taken. All cases of "symptomatic" epilepsy, or cases otherwise complicated, were as far as possible eliminated.

3. The cases have been divided into three series, according as they have responded, successfully or otherwise, to treatment—arrested, improved, and confirmed cases. The influence of the various conditions modifying prognosis has been mentioned in detail, the results of the observations being stated in percentages.

4. A family history of epilepsy will be found more frequently amongst those who have become confirmed epileptics, but an hereditary history of epilepsy does not necessarily militate against the prospects of arrest or improvement of the disease in any given case.

5. The age at the onset of the disease has an especial bearing upon the prognosis. The most unsatisfactory cases are those in which the disease commences under ten years of age; they show the smallest percentage of recoveries and the largest of confirmed cases. If the disease arises between 15 and 20 years of age, an almost equal percentage of arrested and confirmed cases may be expected. The greatest percentage of confirmed cases is found amongst those in whom the disease begins between 25 and 35 years of age, from which time onwards there is a steady increase in the expectations of arrest and diminution in the number which become confirmed.

6. The duration of the malady influences the prognosis

to the extent that arrest, or improvement, is much more likely during the first five than during the second five years. Cases may, however, be arrested even after a duration of from twenty to thirty years.

7. The greatest percentage of confirmed and the lowest percentage of arrested cases occur in those epileptics who are subject to daily or weekly attacks, while conversely the smallest percentage of confirmed and the highest of arrested cases occur in those whose fits are as infrequent as once or twice a year.

8. The character of the seizures influences the prognosis to the extent that the major attacks are the most tractable; then follow combined major and minor seizures; and lastly, the minor attacks occurring alone.

9. Marriage exerts little, if any, influence upon epileptic fits. Some patients are relieved; others are made worse. In the majority of cases the disease remains unaffected.

10. Pregnancy has little influence upon the seizures; at the best there may be only a temporary respite. On the other hand, the puerperium would seem to be especially favourable for the recurrence of fits; while lactation also is not without an exciting influence in their production.

11. The common incidence of epileptic fits is an irregular periodicity. There are types, however, which have been described as "increasing" or "decreasing," according as the fits increase, or decrease, in number in a definite period of time, or in which there is a shortening or lengthening of the intervals between the fits. A case of increasing type may by treatment be converted into one of the decreasing variety.

12. Long remissions, induced either by successful treatment or from spontaneous cessation of the fits, sometimes lasting for several years, are not unusual in epilepsy; they are of favourable prognostic value, but are not synonymous with a cure of the disease.

13. From the collected statistics *a period of arrest for at least nine years has been fixed as the basis upon which*

*a cure of epilepsy may be established. With this definition of a cure I regard 10·2 per cent. of epileptics as curable.*

14. There are some cases of epilepsy which may be regarded as belonging to a curable type of the disease. These present little or no mental impairment, notwithstanding that fits may have existed for a long period. In the cases in which arrest took place, cessation of the fits occurred within the first year of continuous treatment in over 50 per cent.

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## DISCUSSION

Dr. FLETCHER BEACH referred to the statistical observation contained in the paper, that those cases of epilepsy in which there was no heredity improved the most, and pointed out that this was in accordance with the prevalent impression. He asked why those under ten years of age should present such a large number of confirmed cases. The fits that occurred by night were not so frequently arrested as those occurring by day; it was a question, therefore, whether night cases could not be turned into day cases. In regard to marriage, the rule was that the disease was more likely to be transmitted if both parents were affected than if only one; but this did not apply to epilepsy alone. The increase of frequency of fits during lactation seemed to depend on the lowered vitality and strain induced by that process. In regard to menstruation, by many patients its onset had been given as the cause of epilepsy. This was, of course, a mistake. From the results in the paper it would seem that cases must continue under treatment for nine years.

Dr. G. SHUTTLEWORTH, from his experience of epilepsy in children in connection with a large institution, could only record one instance of recovery out of a large number of cases. Further, as one of the medical officers of the London School Board, he had seen some 340 cases of epilepsy in children with a view to determine their educational possibilities. The proportions were, of 340 cases, 17 per cent. were considered fit to continue at the elementary schools; 27.5 per cent. were not fit for ordinary classes, but were intellectually suitable for the special schools, and 40 per cent. were fit only for special institutional treatment. About 13 per cent. were said to be congenital, in 12 per cent. of cases the disease had appeared under one year, 15 per cent. under five years, and 12 per cent. under ten years of age, while only 3 per cent. occurred between ten and fourteen years, most of which were attributed to some traumatic cause. As to the influence of marriage, in many cases an epileptic mother having an epileptic child had got married with the idea of getting rid of the fits herself. Of one family of ten, of epileptic parents, eight had had fits. In only one case was pressure of education assigned as the cause of the fits.

Dr. W. H. BLAKE was impressed with the observation that the curability of the disease was not much greater after than before bromide days. He himself had had very good results with sodium sulphocarbolate and dieting. Presumably the stomach was often the source of peripheral irritation. In cases associated with masturbation where mixed bromides had failed he had had good results with sodium sulphocarbolate, dieting,



and strophanthus. Giving sodium salicylate before the catamenial periods were due had seemed to relieve the fits in those cases apparently associated with menstruation.

Dr. G. NEWTON PITT referred to two points: that there was no greater proportion of cures since the introduction of bromides than previously, and that practically the majority of cases which failed to yield to treatment during the first year were not hopeful. As regarded the number of years of freedom which might be taken as equivalent to cure, it was noteworthy that relapse occurred sometimes even after nine years. It seemed hardly fair to put aside, in estimating cures, all cases that drifted into asylums, as had been done in the paper; they must form a large proportion of the total number of cases in the country. If a patient had had no fit for two years, how much bromide should the patient take after that interval? If there had been freedom for four or five years, should bromide be continued, and if so, how much as the dose? He asked why fits beginning in patients between the ages of thirty and thirty-five should be unfavourable cases.

Dr. BATTY SHAW referred to Sir W. Gowers' statistics that 41 per cent. of cases had an hereditary history of epilepsy, and compared them with Dr. Turner's cases with 37 per cent. He alluded to the difficulties of arriving at trustworthy statistics from observations on out-patients from their ceasing attendance.

Dr. D. A. SHIRRES asked if the toe phenomenon had been investigated in epilepsy by Dr. Turner, also if he had found internal antiseptics of any use in epilepsy.

Dr. TURNER in reply stated that the observations contained in his paper were made on continuous records over a given number of years. He had never investigated the toe phenomenon in epilepsy. The convulsions were, of course, only a symptom of the disease, and a more important element was the mental factor, especially in regard to prognosis. The question of the continuation of the bromide treatment after two, three, or four years of arrest must be gauged for the individual case; as a rule patients objected to the stoppage of the medicine, and often asked to have it recontinued. Twenty grains of bromide might be continued every night for years without causing mental hebetude. He had had no experience of the administration of intestinal antiseptics in epilepsy. As to the statistics before and after the treatment with bromide, they were probably not parallel, in that the definition of cure in terms of years was not known in the earlier cases. The intractable character of epilepsy during the period of growth and educational life was probably due to the mental conditions peculiar to that stage of existence.



A FURTHER REPORT  
ON THE  
REMARKABLE SERIES OF CASES OF MOLLUSCUM  
FIBROSUM IN CHILDREN

COMMUNICATED TO THE SOCIETY BY DR. JOHN  
MURRAY IN 1873<sup>1</sup>

BY  
ARTHUR WHITFIELD, M.D., M.R.C.P.

AND  
ARTHUR H. ROBINSON, M.D., M.R.C.S., D.P.H.

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Received October 31st, 1902—Read March 24th, 1903

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OUR reasons for further referring to these cases are, first, that, owing to the death of one of them in Islington Infirmary, we were able to obtain a supply of material for examination from different parts; secondly, that we had also the opportunity of taking illustrative photographs to show the further development; and thirdly,

<sup>1</sup> 'Transactions of the Royal Medical and Chirurgical Society,' vol. lvi, p. 235.

that, owing to the fact that these cases appear to be unique, it may be of interest to the Fellows of this Society to have their attention again drawn to them.

As thirty years have passed since the able and exhaustive report of Dr. Murray upon these cases, it may be well, perhaps, to very briefly sketch their history. From Dr. Murray's report, and from the verbal communication of a surviving brother, we have found that the father and mother of the patients were cousins on the paternal side, and that the eldest and youngest children of the family, who did not suffer from the disease, were born under

FIG. 1.

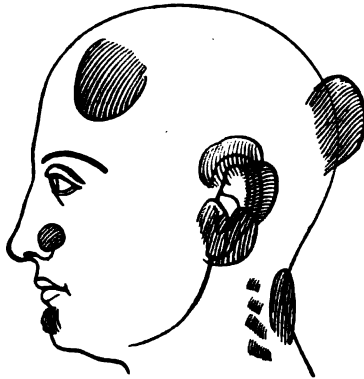


Chart of head, Ellen.

better hygienic conditions than three intermediate children, all of whom suffered from this peculiar condition.

Of these three children we have been able to see two, namely, Ellen, the eldest, who resides at present in the Putney Home for Incurables, and Richard, who died in the Infirmary, and from whom our photographs and material were obtained. We wish to acknowledge our indebtedness to the courtesy of the Matron and Secretary of the Putney Home in allowing one of us to examine Ellen. The third child has, we believe, been dead some time, and we were unable to find more about her than is

contained in Dr. Murray's report. From this report it appears that in the case of Ellen the disease was first noticed at the eruption of the teeth, and did not appear on the skin until she was two years old, while in Richard the gums were observed to be diseased at three months, and the skin at six months.

In reporting the further progress of the two patients whom it was our privilege to see, it will be better to take the female first, as it is to her case that Dr. Murray devotes the greatest attention in his report. From this

FIG. 2



Chart of head, Ellen.

report, and the admirable accompanying illustration, we gather that there has been an increase in the size of the tumours rather than in their actual number, though we find several noted on our charts in positions which are not mentioned by Dr. Murray. Most of the tumours in the previous report were from a pea to a walnut in size; in fact, this latter is the greatest size mentioned. Our charts of the present condition show that the growth of tumours has progressed to such an extent that the patient, instead of presenting a somewhat curious aspect, is now so hideously deformed that she wears her head constantly

bandaged up. The tumours have now the following appearance:—On the forehead there are four, three on the right and one on the left side, that on the left side being about the size of an orange, and all being, as are almost all her tumours throughout, of a deep plum-colour. The ears are so deformed that it is impossible to make out accurately the original anatomical landmarks, but on both sides the aggregated lobed tumours reach a mass the size of the fist. On the left ala nasi and on the chin single tumours are present. The germ of that on the nose is figured in Dr. Murray's illustration, while that

FIG. 3.

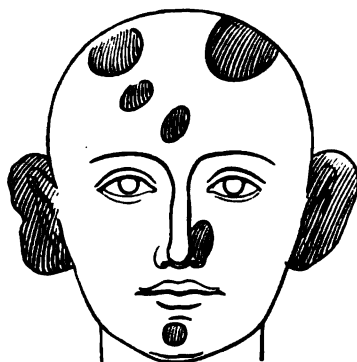


Chart of face, Ellen.

shown in his picture on the right ala nasi has apparently disappeared. He calls it a *verruca plana*, and this might suggest that it was not of the same permanent character as the other tumours; but he also describes that on the right side of the nose as similar, and this is now undoubtedly one of the fibromatous class. The gums apparently remain in much the same state as when he saw them, being mostly covered with small pea-sized fibromata. There is one large tumour on the occipital region, one smaller one, and a double row of quite insignificant ones running down the back of the neck. A large growth, the size of half an orange, lies between the scapulæ, and a few smaller

ones lie about it. The front of the trunk is practically clear. On the extensor surfaces of both elbows there are large diffuent and lobulated tumours, somewhat similar

FIG. 4.

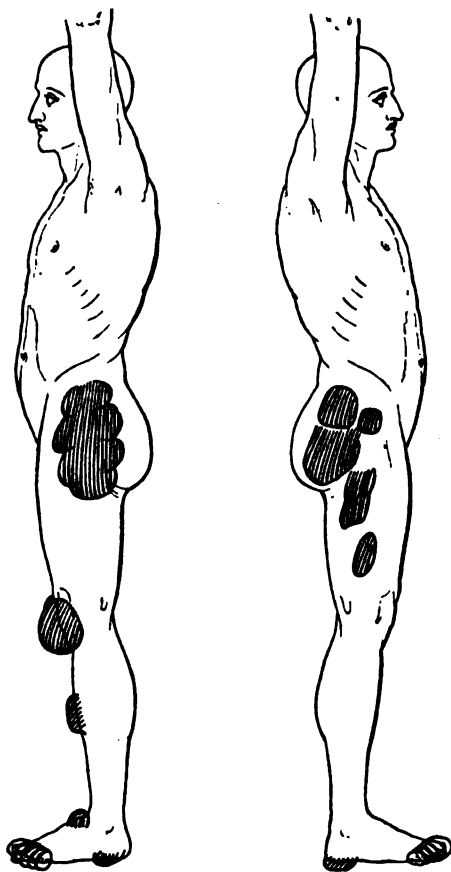


Chart showing distribution of tumours of lower extremities in Ellen.

growths over the extremities of both ulnæ, and the whole of the ends of the fingers of both hands are wrapped in lobed bluish tumours, much resembling those shown in the original picture. The gluteal region is almost entirely

occupied by huge, soft, lobed tumours extending from nearly as high as the posterior superior iliac spine into the upper thirds of the thighs. The trochanter regions are similarly occupied, as is the front of the left knee. There are a couple of growths on the left leg, one in the middle of the shin and one in front of the ankle. The toes resemble the fingers, while on the heels are good-sized growths not finding any parallel on the hands. In hardly any instance can any trace of movement of the skin over the growths be obtained, though they are movable over the deeper tissues. The growths are mostly soft and semi-fluctuating, with dilated vessels coursing over them.

The male patient was less severely affected. His hands, which in Dr. Murray's time only showed slight abnormality, were at the time of his death remarkable, and his scalp showed many tumours not present at the time of the former report. In order to save tedious repetition of the localisation of the tumours, we may say that there were some scattered subcutaneous tumours on the trunk, but none of great size except on the gluteal region, while the feet exactly resembled the hands. With this explanation we think that the photographs will give a far better idea of his unfortunate condition than we are able to do by verbal description.

For purposes of examination pieces were taken from the lobed nasal growth, from the ear, and from one of the fingers. It may be said that, clinically, the growths seemed to differ slightly, those on the nose and ear resembling in appearance and consistency that of ordinary rhinophyma, being completely adherent to the skin, while those on the fingers were stony hard and allowed very slight movement of the skin over them.

With the increased knowledge of the disease formerly known as molluscum fibrosum, and now called neuro-fibromatosis, it became necessary to examine for the presence of nerve-fibres. Specimens were, therefore, specially hardened for the Weigert process, and, owing to the



kindness of Dr. Purves Stewart, we were able to examine sections prepared with a reliable specimen of the stain. Dr. Purves Stewart was also kind enough to look through

FIG. 5.

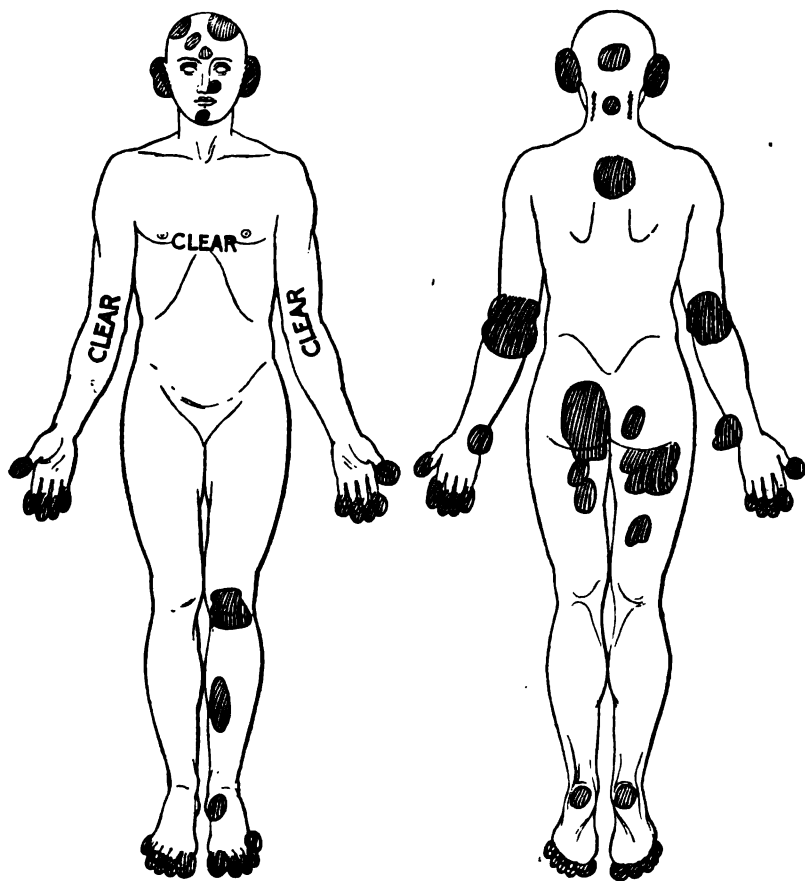


Chart showing distribution of tumours on body and extremities in Ellen.

the sections with one of us, but in no instance was a nerve-fibre found.

Other specimens were stained with a variety of the ordinary histological stains, including that for elastic

tissue, but none was found in any of the tumours. In the case of the finger tumour the growth was found well circumscribed, and only lightly attached to the overlying skin and deeper tissues. All the ordinary appendages of the skin were almost normal, but pushed up and slightly compressed, none being found enclosed within the tumour. The tumour itself was composed of dense fibrous material, which in some parts showed well-developed fibrous tissue, rather rich in cells, while in others it had a hyaline structure with rather large cells, lying in more deeply stained substance bearing a strong resemblance to cartilage, though we feel certain that no cartilage was present. The tumours from the ear and nose were so similar that it was only by the shape of the pieces that we could easily tell them apart. In both cases the growth was far more diffuse, blending intimately with the overlying skin. Here in most cases also the skin appendages were pushed up, but in one section a part of a hair-follicle was found enclosed in the tumour. The fibrous element was much less marked in these growths than in that from the finger, and the whole may be said to be formed of a hyaline ground substance, in which were numerous fine fibrils of collagen and packets of connective-tissue cells, the latter lying for the most part in spindle-shaped groups surrounded by fairly well formed and dense fibrous tissue. These collections of cells probably really represented long bands of cells which were cut across obliquely. In all cases there was seen to be a distinct tendency of the tumours to form separate lobes, and this was well shown in the microscopic sections; a concentric outside with radial central arrangement of the fibres was most usually found. All the tumours were very vascular, but those from the nose and ear especially so, the vessels in every instance being provided with a thin but well-organised wall. The hyaline ground substance was investigated by means of several stains, but without very definitely ascertaining its nature. It was apparently not myxomatous in nature, as it gave no metachromatism with

*Robinson and Whitfield: Molluscum Fibrosum in Children, Plate I.*



PHOTOGRAPH OF RICHARD.  
Showing deformity of nose and curious condition of fingers.



*Robinson and Whitfield: Molluscum Fibrosum in Children, Plate II.*



PHOTOGRAPH OF HEAD OF RICHARD.  
Showing deformity of left ear.





Subcutaneous node from dorsal surface of the finger.







Subcutaneous growth from the ear.



thionin. On the whole the best specimens were obtained with Hansen's modification of Van Gieson's stain. We are quite aware that in making this further report we have not advanced in knowledge of the pathology or etiology of this remarkable disease. We think, however, that it should be taken out of the class of molluscum fibrosum, which is now practically synonymous with neuro-fibromatosis, a disease with which this has apparently nothing in common, and placed simply in the category of multiple fibromata.

## DISCUSSION

Sir THOMAS BARLOW had had these cases under his observation for many years after the death of Dr. Murray. In regard to the etiology, Dr. Murray had thought the tumours due to insanitary conditions, but years after the birth of the children the father came under observation with undoubted malignant disease, and died from cancer of the stomach. The eldest of the children was certainly the most severely affected, and the youngest was least, and in her the disease was not progressive, as it was in the former two cases. Each of these children was liable to inter-current febrile attack, in some cases with increase in the size of the tumours and attacks of dermatitis. In one case, after removal of a tumour surgically, there was very alarming surgical fever. The mental condition of the eldest patient was defective, and there was deafness. The defect was less in the second, and least in the youngest.

Dr. ROBINSON, in reply, said that the mental condition of the patient whom he had seen was similar to that of the eldest sister as described by Sir Thomas Barlow.

A REPORT ON FOUR CASES  
OF  
ACUTE SEPTIC INFLAMMATION OF THE THROAT  
WITH BACTERIOLOGICAL EXAMINATION  
OF EACH

*A Sequel to a similar Paper read by* SIR FELIX SEMON,  
*April, 1895*

BY  
PHILIP R. W. DE SANTI, F.R.C.S.  
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WESTMINSTER HOSPITAL

Received May 1st, 1902—Read February 10th, 1903

IN an extremely able and important paper, read by Sir Felix Semon before the Fellows of the Royal Medical and Chirurgical Society on April 23rd, 1895, and entitled "On the Probable Pathological Identity of the Various Forms of Acute Septic Inflammations of the Throat and Neck hitherto described as Acute Œdema of the Larynx, Œdematous Laryngitis, Erysipelas of the Pharynx and Larynx, Phlegmon of the Pharynx and Larynx, and Angina Ludovici," the author very clearly points out the extreme confusion that exists in the nomenclature and

classification of these inflammations, and expresses his conviction "that the various forms of acute septic inflammations of the throat and neck, hitherto considered as so many essentially different diseases, are in reality pathologically identical; that they merely represent degrees varying in virulence of one and the same process; that the question of their primary localisation and subsequent development depends, in all probability, upon accidental breaches of the protecting surface through which the pathogenic micro-organism which causes the subsequent events finds an entrance; and that it is absolutely impossible to draw at any point a definite line of demarcation between the purely local and the more complicated, or between the œdematous and the suppurative forms."

To prove these convictions he gives clinical details in order of ascending severity of fourteen cases which had come under his own personal observation, but, at the same time, confesses that bacteriological evidence in his cases is unfortunately conspicuous by its absence.

He also expresses a hope that subsequent observers will test the correctness of the views put forward by himself as to the probable identity of the various acute inflammations of the throat and neck.

Since the reading of Semon's paper I determined in any case of acute septic inflammation of the throat that might present itself to my notice to keep a careful record, and to test, if possible, the nature of each case bacteriologically, so that if I had a sufficiency of cases I might be enabled to come to some definite conclusions either for or against Semon's views, which views, at the discussion which followed his paper, were more or less fiercely attacked.

My experience since 1895 of these so-called acute septic inflammations of the throat and neck has been limited to four very distinct and definite cases, notes of which I herewith give, according to Semon's plan, in their order of ascending severity.

CASE 1.—A male patient, aged 48, came under my care as an in-patient at Westminster Hospital the 10th May, 1899, with a deep-seated cervical abscess reaching from just below the right mastoid process to the level of the cricoid cartilage, and extending under the right sterno-mastoid muscle to near the mid-line of the neck. There was a history of old suppuration of the right middle ear, and pressure on the cervical abscess caused pus to well out of the right external auditory meatus. An examination of the tympanum showed complete absence of the membrana tympani: there was some pain caused by pressure over the mastoid process, but there was an absence of any redness, swelling, or œdema over the process. I suspected a perforation of the mastoid process on its deeper digastric aspect (Bezold's perforation), and considered the deep-seated cervical abscess to be due to infection through this perforation.

I opened up the mastoid antrum and cells, evacuated pus and granulation tissue, and found a somewhat ragged aperture on the deeper aspect of the process communicating with the abscess in the neck. The mastoid and cervical abscesses were both thoroughly opened and drained, and the patient progressed favourably until June 2nd, on which day the temperature rose to 102° F., and there was general malaise and pain. Three days later cutaneous erysipelas commenced on the left cheek; later on the same day it had spread to the left side of the neck, the whole left side of the face, and also across the middle line of the face and neck to the right side.

There were also patches of redness all over the back down to the lumbar region. In the evening the temperature was 103·4°, and the man was very ill. Soreness of the throat was complained of, and examination showed a bright red swollen condition of the posterior pharyngeal wall, and of the whole of the soft palate, especially the uvula. Cultures from the mucus of the throat showed mainly *Streptococcus pyogenes* with some staphylococci.

Antistreptococcus serum, 10 c.c., was injected into the abdominal wall June 2nd.

June 3rd.—Twelve noon another 10 c.c. was injected. Swelling of the eyelids and throat less.

4th.—Face less swollen, also eyelids. Rash almost entirely gone from the back. Temperature in the evening  $101.6^{\circ}$ . Ten c.c. of serum injected. Temperature fell at midnight to  $99.2^{\circ}$ . Urine normal.

5th.—Cheeks still red but less swollen. Rash almost gone from the rest of the face and neck. Throat still red but not swollen.

6th.—General improvement.

7th.—Desquamation. Throat normal. From this date the patient made an uninterrupted recovery.

CASE 2. *Acute œdematous tonsillitis and pharyngitis*.—A man aged 32 attended my out-patients' in 1898 at Westminster Hospital complaining of swelling in the neck and sore throat. His illness had started with headache, shivering fits, and sickness three days before I saw him. These symptoms were soon followed by much pain and dryness in the throat, the pain, especially on swallowing, having greatly increased for the last twenty-four hours. For two days there had been weakness of the voice, and the patient could only just use his voice in a whisper.

The man looked ill, his temperature was  $104.6^{\circ}$ , his pulse rapid (120) and compressible, and there were enlarged and tender glands on both sides of the neck. The urine was normal.

Examination of the throat showed intense redness and swelling of the right tonsil, of the whole of the soft palate and uvula, and a dark red glazed and swollen condition of the posterior pharyngeal wall. There was also slight œdema of the epiglottis, but the rest of the larynx which could be fairly seen was neither congested nor swollen. Swab cultures were taken from the tonsil and pharynx, and examination by the pathologist showed *Streptococcus pyogenes* infection.



I advised the patient to come into the hospital at once but although the gravity of the case was clearly put before him he refused and left the hospital. I never saw him again, and the subsequent history of the case is therefore unknown to me.

*CASE 3. Acute gangrenous inflammation of the throat.*—A man aged 21 came to my throat clinic at Westminster Hospital December 2nd, 1901, complaining of sore throat, pain and great difficulty in swallowing, loss of voice, and general malaise. His throat trouble had commenced two days previously, and he had rapidly got worse. He could not in any way account for his illness, there being no history of injury, old ulceration of the throat, or of any people in the house he lived in suffering from throat trouble. The patient worked in an oil-shop and was indoors most of the day. He had had influenza six years previously, and had had slight sore throat once or twice since, but had got quite well in a day or two after using chlorate of potash gargle.

The patient's condition when seen by me in the Out-patient Department was as follows :

Patient looks very ill and pale, and complains of aching pains all over. His temperature is  $101.2^{\circ}$ , pulse very frequent (120) and soft. Can only speak in a whisper and with difficulty ; no dyspnoea present. Urine normal.

•

*Examination of Pharynx and Larynx.*

The uvula was enormously swollen, intensely red, and the lower half black and gangrenous.

The inflammation at the base of the uvula had spread to the soft palate, which was red and cedematous, and to the tonsils, the latter being similarly affected but to a less degree.

The posterior pharyngeal wall was red and slightly swollen.

Laryngoscopic examination showed the epiglottis to be slightly swollen, especially at its base, and there was very extensive œdematous swelling of the left ary-epiglottic fold, the latter looking like a large yellowish polypus; the right half of the larynx was unaffected.

The patient was at once admitted. On admission it was found that he could not swallow at all, not even liquids.

A swab culture from the uvula revealed the presence of *Streptococci pyogenes*, and some staphylococci; no diphtheria bacilli.

Immediately after admission the house physician, Dr. Watson, injected into the right lumbar region 20 c.c. of antistreptococcal serum. Locally, pure carbolic acid was rubbed into the gangrenous uvula, and frequent inhalations of Vapor Creasoti were ordered. The patient was also put on fifteen-minim doses of the Liq. Ferri Perchloridi every four hours. For the painful deglutition spraying with a 10 per cent. solution of cocaine was ordered.

Five hours after admission the patient was able to swallow some milk.

December 3rd.—Patient felt much better, and was able to take fluids more easily. Temp. 100°. No more serum given. The gangrenous mass on the uvula showed a line of demarcation.

4th.—Improvement maintained. The uvula looked more healthy. Pure carbolic acid was re-applied. There was still very marked œdema of the uvula, palate, and ary-epiglottic fold.

6th.—Patient able to take bread and butter, Benger's Food, etc. Uvula much reduced in size, and the gangrenous slough had come away. The voice was beginning to improve. Temperature was 99.6°.

10th.—The patient was almost well, and taking full diet. The uvula was of normal size, but there was still some œdema of the larynx.

20th.—Patient left the hospital quite well.

I subsequently saw him on three or four occasions, and found the throat quite normal.

**CASE 4.** *Acute pharyngitis due to Streptococcus pyogenes followed by septicæmia, deep glandular inflammation, and pericarditis.*—This case was under the care of my friend and colleague Mr. W. G. Spencer, but I had the opportunity of seeing the man whilst in the hospital, and I must thank Mr. Spencer for his courtesy in allowing me to refer to the case.

A man 21 years of age was first taken ill October 16th, 1898, with a sore throat, followed by swelling in the neck. He gradually got worse and was admitted into Westminster Hospital, where he was first seen by Mr. Spencer on October 24th.

The patient was then partly unconscious, had great pain and difficulty in swallowing, and kept placing his hand over his heart where he felt great pain. The temperature was  $101.4^{\circ}$ , having been  $103^{\circ}$  during the night; the pulse was 120, small, and of low tension; respirations 30 and quiet. The mouth could only be partially opened; the tongue was swollen and brown, and the posterior pharyngeal wall was covered with brown sticky mucus, but no membrane. The left side of the neck was much swollen, red, brawny, and cedematous. An incision had been made by the house surgeon at the posterior border of the sterno-mastoid muscle, from which a sanious fluid had escaped, but no pus.

On auscultation a loud pericardial friction rub could be heard.

The mucus from the throat and the discharge from the wound in the neck were examined by Dr. Blaxall, the bacteriologist, and he found both in cover-glass specimens, and upon cultivation, mainly *Streptococci pyogenes*. In the cultivation from the throat a yeast, *Staphylococcus albus*, and a few bacilli were also found.

At 9.30 p.m. on the 24th, eight days after the first signs of the illness, 10 c.c. of antistreptococcal serum

were injected, a second dose at 6 a.m., and a third at 4.20 p.m. on the 25th, and a fourth on the 26th. The effect was remarkable, the patient beginning to rally at once.

On the 27th the temperature fell to  $98^{\circ}$ , and did not rise above  $100.8^{\circ}$ . The pulse was fuller and of greater tension; the patient was conscious and had no pericardial pain. The tongue was less swollen and more moist, and the pharynx was in a cleaner condition. The incision in the neck was discharging pus from deep-seated glands.

On the 31st no pericardial friction-sound could be heard, but there was a marked pleural rub extending from the cardiac area upwards above the third left rib. On November 5th no abnormal sounds could be heard, but there was some impaired resonance above the third left rib.

The patient left the hospital on December 14th to go to a convalescent home, the pulse and temperature being then normal, and the wound in the neck healed.

This case is published in the 'Lancet,' January 21st, 1899, under "A Mirror of Hospital Practice."

These four cases, brief notes of which I have given, constitute the series of acute septic inflammations of the throat and neck that have come under my personal observation since 1895. They are a series smaller, of course, in number, but quite parallel with Semon's cases. They were all four very marked types, and therefore easy to diagnose. I have no experience of the very mild yet distinct cases related by Semon.

In Case 1 there was redness, swelling and œdema of the soft palate and pharynx, not intense, but quite definite, and forming part of an attack of ordinary cutaneous erysipelas of the face, neck, and back.

In Case 2 there was similar swelling, but the right tonsil and the epiglottis were involved, and the swelling of the affected parts was very much more intense, and the patient's general condition more grave than in

Case 1. It is a matter for regret that the further history of the patient was unobtainable.

In Case 3 the uvula was the part chiefly attacked, and the inflammation was of the worst description, namely, gangrenous.

In Case 4, that of Mr. Spencer's, there was a severe septic pharyngitis with deep-seated inflammation of the neck and pericarditis.

I think it will best serve my purpose if I now proceed to take up one by one the four important objections that Semon stated he was conscious might be raised against his views on acute septic inflammations of the throat and neck, and analyse them in the light of the experience offered by my above four cases.

*Objection No. 1.*—"That he had given no proof that the milder cases in his series were really of septic origin, and that they might well have been simple catarrhal inflammation."

It is obvious that without any adequate and expert bacteriological examination of these milder cases—and Semon admits the absence of a bacteriological examination—it is open to any critic to deny the certainty of their septic origin, and to conclude that from the mildness of the symptoms the cases were clinically catarrhal inflammations pure and simple.

In so far as my four cases go, have I any proof (a) bacteriological, (b) clinical, to bring forward for or against Objection No. 1?

Of my four cases, two in my opinion are analogous to Semon's milder cases, namely, my first case, in which the patient suffered merely from swelling and redness of the uvula, soft palate, and pharynx, but in which the sore throat, such as it was, was undoubtedly of septic origin, being part of a definite extension of a well-marked case of cutaneous erysipelas to the throat, and in which a cultivation from the throat showed *Streptococcus pyogenes* infection; and my second case, exactly analogous to No. 4 in Semon's series as regards the parts attacked,

namely, the tonsil, pharynx, and epiglottis, and in which a cultivation again showed streptococcal infection.

Now I consider these two cases, in which the bacteriological examination was made by an expert, and in both of which streptococcal infection was found, and in both of which the symptoms were, especially in the first case, of a more or less mild character locally, prove undoubtedly that Semon's milder cases were probably of a septic nature, as suggested by him; and this is further strengthened if we look at the cases from their clinical aspect. These milder cases, as well as the more severe types of acute septic inflammations of the throat, are characterised by their sudden onset, rapidity of progress, absence—as a rule—of any demonstrable cause, the limited distribution of the inflammation in contradistinction to the more general distribution in catarrhal conditions, the much greater amount of œdema and redness, and the well-marked and severe constitutional symptoms.

In both my first and second cases these characteristics were well marked in every way, and I conclude, as regards Objection No. 1, that bacteriological investigation has proved that these milder cases can be of septic origin, and that the clinical symptoms are distinct from those of a catarrhal inflammation.

*Objection No. 2.*—"That the different localisation in Semon's cases, namely, whether originating in the pharynx, larynx, or cellular tissue of the neck, spoke against their being identical."

This objection, I consider, cannot possibly hold good: the different localisation of these septic inflammations of the throat must surely depend on the resisting powers of the parts attacked, an accidental breach of surface, possibly quite minute, or a pre-existing condition of catarrh, rendering the part more susceptible to infection.

As pointed out by Semon, diphtheria remains diphtheria whether it primarily attacks the tonsils, pharynx, nose, conjunctiva, or vulva; and it is the same with these acute septic inflammations of the throat.

In my four cases the posterior wall of the pharynx was primarily attacked in two, the tonsil in another, and the uvula in the fourth case, yet they were all identical diseases, as proved by their bacteriological results, and they only differed clinically in so far as the severity of the symptoms varied.

It is, I think, fairly certain that the tonsils are particularly likely to be the primary seat of these inflammations by virtue of their anatomical arrangement: that this is so in regard to other infectious diseases, notably diphtheria, is well known, and within recent times ample bacteriological evidence has been brought forward to prove that in tubercular infection of the cervical glands the tonsils have been often, if not mainly, responsible for the entrance to, and infection of the cervical glands by the tubercle bacillus.

I am not dealing in this communication with the disease described as Ludwig's angina, or, as I prefer to call it, submaxillary cellulitis; but I would say incidentally that I have had under my care some six or more such cases, and in so far as my memory serves me, in three or four it was definitely made out that the infection started from a lesion in the floor of the mouth. There are no records of the bacteriological examination of these cases.

*Objection No. 3.*—"That the variations in the fever curve in Semon's individual cases also seemed to point in the direction that this fever was caused by different and not identical processes."

Of my cases, No. 1 presented a temperature of the usual type that accompanies an attack of cutaneous erysipelas, and its course was characteristic of that disease, except in so far as it was affected by the injections of the anti-streptococcus serum. In case No. 2 I only saw the man once, and the subsequent history is unknown, but on the occasion I saw the patient the temperature was  $104.6^{\circ}$ .

In case No. 3 the temperature was  $101.4^{\circ}$ , but after the

first injection of antistreptococcus serum never rose above 100·6°.

In Case 4 the temperature, previous to the injections, was over 103° F., and subsequently did not rise above 100·8°.

The temperature in these four cases varied, therefore, between 104·6° and 101·4°, and although I consider that the temperature in this class of case is bound, as in other similar diseases, to vary, especially according to the resulting inflammation, whether œdematous, suppurative, or gangrenous, and according to the amount of the poison absorbed, yet I venture to think that further observations will prove that these acute septic inflammations of the throat are almost invariably accompanied by some degree of more or less severe fever.

At any rate, in the limited number of cases I have seen there has always been fever, although no fever curve that I could adjudge characteristic of the disease in question; yet I consider all my cases identical in nature.

*Objection No. 4.*—"That the fact of the exudation sometimes being of a serous and sometimes of a purulent character most powerfully combated the view that these inflammations were identical in nature."

This objection has to be investigated entirely from a bacteriological point of view.

Years ago I was taught, and have since myself taught that erysipelatous affections were of three kinds—cutaneous, cellulose-cutaneous, and cellular; and that the differences between them were partly bacteriological, partly clinical.

Cutaneous erysipelas was looked upon as being due to a specific micro-organism, the *Streptococcus erysipelatis* of Fehleisen, and it was taught that this micro-organism, if inoculated experimentally, produced cutaneous erysipelas, and that alone, and not the other two varieties; and that the cellulose-cutaneous variety and cellulitis were due to a mixed infection, and differed clinically in the fact that the two latter varieties ended in suppuration, and that



between the two the clinical difference existing was that in cellulito-cutaneous erysipelas the skin and cellular tissue were affected simultaneously, whereas in cellulitis the skin was affected secondarily.

Now this was the teaching, I believe, from 1888 up to at all events 1893.

Now do these views hold good at the present time? Unhesitatingly I would answer this in the negative. Even during the period when this teaching was almost universal doubts had been cast on Fehleisen's experiments and conclusions, and other observers had failed to substantiate the specificity of Fehleisen's *Streptococcus erysipelatis*.

To prove conclusively the specificity of Fehleisen's streptococcus it was necessary to show that this micro-organism, and it alone, could produce cutaneous erysipelas in the human subject, and that no other micro-organism could produce the disease.

Proofs against these specific results were soon forthcoming. It was found that the *Streptococcus pyogenes* could also produce the disease, and that other pyogenic micro-organisms could produce the same result.

Taking up a recent and well-known manual on bacteriology, *i. e.* Muir and Ritchie's, I find it stated (page 155) of the *Streptococcus pyogenes*, "It has been proved by Marmorek's experiments and those of others that the same streptococcus may produce at one time merely a passing local redness, at another a local supuration, at another a spreading erysipelatos condition, or, again, a general septicæmic infection according as its virulence is artificially increased. Such experiments are of extreme importance as explaining to some extent the great diversity of lesions in the human subject with which streptococci are associated."

And again, "Nearly all observers now agree that the *Streptococcus pyogenes* and *Streptococcus erysipelatis* are one and the same, erysipelas being produced when the

*Streptococcus pyogenes* of a certain standard of virulence gains entrance to the lymphatics of the skin."

Now these statements, taken from a recent standard work on bacteriology, appear to represent the present-day opinion of those authorities best calculated to form competent conclusions on the matter, and amount, in my opinion, to this :

(1) That the *Streptococcus pyogenes* and other pyogenic cocci can produce, apart from purulent inflammation, all other forms of inflammation, such as serous, fibrinous, hæmorrhagic, and gangrenous inflammations.

(2) That the variety of inflammation resulting depends (a) on the quantity, (b) the virulence of the organism introduced into the system, (c) the resisting power of the subject inoculated.

It seems to me, therefore, that these conclusions are amply sufficient to account for the differences in not only the fever curve of these various septic inflammations of the throat, but also for the differences in the kind of inflammation resulting, namely, œdematous, purulent, or gangrenous. .

From what I have now said it will be obvious that I am in entire agreement with the views put forward by Semon in his paper on "Acute Septic Inflammations of the Throat," and that my agreement with his views has been strongly supported by the results, bacteriological and clinical, of my four cases.

I have, at any rate, brought forward evidence that in all four of my cases the *Streptococcus pyogenes* was present, and that the treatment of three of the cases with antistreptococcus serum was attended by the happiest results.

I desire now just to say a few words as regards the treatment of this class of case.

*Treatment.*—In all cases suspected to be of the nature of an acute septic inflammation of the throat it is absolutely essential to have a competent bacteriological examination made of the secretions, both cover-glass and culture

preparations being made, and if possible inoculation experiments carried out. If bacteriological investigation prove the presence of the *Streptococcus pyogenes* there should be no delay in injecting the patient with the anti-streptococcus serum. The marvellously good results that ensued in the almost hopeless case, No. 4 of my series, from the injection of this serum, together with the equally good results accruing from the same treatment in Cases 1 and 3, leave no doubt in my mind that in cases in which the streptococcus is found we have a most efficacious remedy in antistreptococcus serum; and I feel sure that in the fatal cases recorded by Semon the results might have been different if this treatment had been in vogue and carried out. It is, however, most necessary to emphasise the fact that unless the streptococcus is identified as the cause of the disease it would certainly be useless, and, indeed, extremely hazardous to use the streptococcal antitoxin. For its success the *Streptococcus pyogenes* must be discovered in the secretions of the affected part or parts.

The dose to be injected depends on the age and condition of the patient: in an adult I consider 10 to 20 c.c. sufficient as an injection; in children the dose should be proportionately smaller.

In addition to streptococcal antitoxin injections I think the free administration of large doses of the Liq. Ferri Perchloridi of service.

If œdema be very marked, and especially if the larynx be attacked, free scarification should early be resorted to, and tracheotomy performed as soon as the breathing becomes markedly embarrassed.

If the inflammation be gangrenous, the gangrenous parts other than the larynx itself should at once be thoroughly rubbed over with pure carbolic acid; this local treatment had excellent results in my Case 3.

These are the main lines of treatment I would advocate. Among adjuncts are the administration of stimulants according to the state of the pulse, the use of disinfecting vapours, such as the Vapor Creasoti, and the spraying of

the throat before the ingestion of food with cocaine or cocaine and menthol sprays.

The external application of cold by means of ice coils, etc., to the neck I deprecate, as I hold that these cold applications only tend to further devitalise already damaged tissues.

In similar diseases, especially of an erysipelatous nature, attacking other parts of the body, cold applications are contra-indicated, especially if suppurative or gangrenous inflammation threatens or has already ensued.

## DISCUSSION

Dr. DE HAVILLAND HALL said that, as he had opened the discussion on Sir Felix Semon's paper in 1895, it seemed not unfitting that he should be the first to speak on the present paper. He considered that it was of great importance to have a bacteriological examination made in all cases of acute septic inflammation of the throat. Such cases were particularly distressing from the rapidity of onset and the fatal result if not suitably treated. In one of the cases recorded in the paper which he had seen the prognosis seemed in the highest degree grave, and yet recovery occurred. It was difficult when the former paper was read to fall in with the idea of a pathological identity, but now a bacteriological identity had been established the unity of the cases was more manifest. Was it not possible that other micro-organisms than the *Streptococcus pyogenes* might be concerned in producing clinically similar results? The late Dr. Kanthack had shown that ulcerative endocarditis might be due to a number of different organisms, and thus, although these cases were identical clinically, they were not so pathologically. Allusion was made to a case of throat inflammation in a child resembling diphtheria, but no diphtheria bacilli were found, only staphylococci; this was followed by two other cases in the same house, one of which proved fatal, in neither of which was the diphtheria bacillus found.

Sir DYCE DUCKWORTH considered that Sir Felix Semon's original paper opened a new chapter in throat inflammations, and now that bacteriological evidence of their unity had been brought forward the subject assumed great importance. The specificity of the antitoxin treatment raised the question of polyvalency and the need for a mixed antistreptococcus serum. He had never seen any harm come from its injection. There was little doubt that septic inflammations of the throat might arise from many varieties of streptococci, differing both morphologically and in virulence.

Mr. E. B. WAGGETT observed that in each of the cases quoted the subject was a man in the prime of life; in his own cases the same thing was observed, and not only so, but the subjects were in excellent health. Details were given of some of his cases. In one case, arising without obvious cause, the patient, a young man, became practically moribund; during the first three days of illness there was sore throat, but no severe symptoms; on the fourth day, however, the fauces were almost completely blocked, but the larynx was not affected. Evacuation of inoffensive pus by an incision in front of the sterno-mastoid was followed by

speedy recovery without injection of antistreptococcus serum. The case emphasised the necessity for operating immediately. The *Streptococcus pyogenes* was found in almost pure culture. The serious character of the disease seemed to be due to the virulence of the organism concerned.

Dr. DUNDAS GRANT held that the importance of recognising these cases was enormous. It was necessary to decide whether the local or constitutional symptoms were most urgent in regard to the management of the cases. In many the morbid appearances in the throat were comparatively slight, but danger was present from blood poisoning. As to diagnosis, with a sore throat and bodily illness, and a voice suggesting peritonsillar abscess, but with ability to open the mouth and with nothing to be seen in the throat—with such conditions the danger to life was great. A case of this kind was described which proved fatal from laryngeal obstruction and cardiac failure. Too great precaution was hardly possible. The constitutional symptoms might suggest a correct diagnosis when throat changes were all but absent. Certain cases simulating diphtheria were, on the whole, the most favourable. Antistreptococcus serum was of great value in this group of cases; he had not himself seen any harm from it, and he would inject it early in cases of doubt. It was of the utmost importance to keep up the patient's strength, and especially to ward off heart failure. Cold treatment was, in his opinion, advantageous.

Dr. F. J. POYNTON thought the paper had an important bearing on the unity of streptococcus infections, but there was such a thing as a false bacteriological clearness. It was doubtful whether the organism described was really *Streptococcus pyogenes*. To distinguish between the varieties of *Streptococcus pyogenes* it was necessary to employ other methods than cultivation and the consideration of morphological characters,—as, for example, experimental injections and such bio-chemical tests as Marmorek's filtration test, investigations on hæmolysis, bacteriolysis, agglutination, and specific immunity. If the unity of the streptococcus was accepted in the present state of knowledge he thought that the result would be to attempt to explain clinical difficulties by referring them to an insecure bacteriology. He would accept for argument's sake this unity, and turn to the explanation that was then given of the differing clinical results. They were explained by (1) the number of organisms that gained access; (2) the intensity of the virulence; and (3) the resistance of the individual. But were these sufficient? He thought not, and detailed a recent investigation he made on this subject with Dr. A. Paine. A student pricked his finger at a post-mortem examination on a case of suppurative peritonitis; he developed alarming symptoms, and was threatened with acute septicæmia. Fortunately his resistance proved successful, though an abscess

developed in the axilla; from the pus they obtained an organism which might be justly called the *Streptococcus pyogenes*. At the same time they isolated a streptococcus from a case of malignant endocarditis. Both these they placed in the same medium, a slightly acid one (not the most favourable for maintaining the virulence); thence they transferred them to blood-agar. Two rabbits living under the same conditions and from the same litter were inoculated intra-venously with these results. A small dose from the septic case produced death in twenty-four hours with septicæmia; a large dose from the case of endocarditis produced death in five days from malignant endocarditis of the mitral valve, the specimen of which he showed. Wherein lay the explanation of the different results? Not in (1) the number of organisms injected, for the fewer organisms produced the most fatal result; probably not in (3) the nature of the resistance, since the two rabbits were much alike; but very plausibly in (2) the difference of virulence. They carried on the original cultures in the acid medium for three weeks and repeated the investigation. One rabbit was injected intra-venously from the septic micro-organism, and one subcutaneously, and two more in the same way with the organism from the case of endocarditis with these results:—The two rabbits injected with the septic micro-organism died on the second and tenth day respectively from septicæmia; the rabbit injected intra-venously with the other microbe died on the fourteenth day from malignant endocarditis of the aortic and mitral valves; that injected subcutaneously developed a firm nodule at the point of inoculation, which disappeared, and the animal recovered. They waited another three weeks and again repeated the investigation, and this time all the animals recovered. He thought then that factor 2—the intensity of virulence—had been altered in each case to practically a zero. He believed there was a fourth factor, viz. a tendency inherent in micro-organisms to produce special poisons, a specific toxicity which had to be reckoned with in all investigations on the unity of the streptococcal group.

Sir FELIX SEMON said that when he brought forward his paper in 1895 it had met with considerable opposition, and he believed that arose, firstly, because the diseases which he had classed together had always been considered so entirely different clinically; secondly, because he had used the words "pathological identity," meaning thereby the same morbid process, and not the identity of the micro-organism; and thirdly, because of the uncertain state of bacteriology at that time. Now, as then, it was clear that it was impossible to draw a sharp line between the different clinical varieties of acute septic inflammation of the throat. Any of the group of pyogenic organisms might, he had contended, produce inflammation of this type. It was the identity of the pathological processes produced by many kinds

of organisms that he had upheld. While in some cases there had been sugar in the urine, as a rule the general health was excellent. Since 1895 he had seen five more cases; in one permanent deterioration of health had resulted; in another case a fatal result ensued after tracheotomy; in a third after tracheotomy death also occurred (in this antistreptococcus serum was not employed); in another, in which symptoms of general poisoning of the system developed, antistreptococcus serum was injected and transfusion employed; in the fifth case *Streptococcus pyogenes* was found, and the antistreptococcus serum was injected, with recovery after a protracted illness. The prognosis in the severer cases was very grave. He was in favour of using antistreptococcic serum, but as he believed there was a specificity in the sera, and that the disease might be caused by any one of the pyogenic groups, the sera would not be equally beneficial in all cases. If the streptococcus could not at once be searched for from any cause was the serum to be injected? In any desperate case under such circumstances he thought it should.

Mr. DE SANTI, in reply, remarked that the subjects of angina Ludovici which he had seen were unhealthy and alcoholic, although the other conditions occurred in healthy subjects. He also would employ the antistreptococcus serum in cases of doubt without waiting for a bacteriological examination.



# RISE OF BLOOD-PRESSURE IN LATER LIFE

BY

PROFESSOR T. CLIFFORD ALLBUTT, F.R.S.

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WHEN in the third quarter of the nineteenth century I entered the profession of medicine physicians were much occupied in the deadhouse, contemplating the ruins of mortality. Surrounded by the last dilapidations of the human frame, they laid bare almost daily in its inward parts some previously unknown wreck, blight, or decay. In the wards, meanwhile, before Darwin's theory had changed the habit of thought, the mind of the physician was coloured by notions of the fixity of kinds; he was apt to attribute a certain fixity even to the species of disease, especially to those kinds which, as the phrase ran, were organic rather than functional. Functional diseases made no appearance in the deadhouse; indeed, many of the acute diseases had proved, in recent experience, to be, if often violent, yet temporary oscillations, tending, if let alone, to recovery. The end of chronic visceral disease, however, seemed to be inevitable death, in derision of drugs. Thus it happened that to organic diseases, too rigidly conceived as entities, names derived not from original causation or clinical character, but from

the ultimate forms of destruction, became attached ; and I well remember, as a student, how one distinguished teacher and another would display a shrivelled kidney or liver, a distorted heart, or a softened brain, and ask disdainfully of what use medicines could be for such degradations, even in their earlier stages ; how organs with such proclivities were to be converted by prescriptions ? Not more than fifteen years ago I said to a late physician, one of the ablest of the last generation, " I am sick of diseases, I want to know origins and processes." We were walking together, and he, stopping, turned upon me and exclaimed, as if new light were breaking in, " Processes ? ah, processes ! Yes, the pathology of processes is the work of the future." I had urged, for example, that bloated or withered kidneys are not engendered of vice in the kidneys themselves, but of the prolonged, uniform, symmetrical action upon both of them of some unknown poison or poisons circulating in the blood ; an influence, furthermore, by no means confined to these organs, but visible in wide-spread effect elsewhere in the body : that to speak of such cases as cases of kidney disease is therefore misleading ; and so on of other post-mortem wreckage. The discovery of such utter mischief after death is matter not for our despair, but for our disgrace ; it is not a declaration of the impotence of therapeutics, but black evidence of our blindness and negligence in the past history of the individual. With the pathology of the dead we have made great way, the pathology of the living is hardly begun.

These arguments, sir, may seem to savour of platitude, but I think even to-day that they have not lost their application ; that you will not find it hard to carry your mind back so far as to realise the change—the transformation—which is passing over medicine at this time, and that you may find it still less difficult to accept at my hands some attempt to study disease at its sources rather than at the term when its work is done.

To my friendship with the late Dr. Mahomed I owe

much of my conviction of the clinical value of the study of arterial pressures; and a few years later I was encouraged and aided in this study by the late Professor Roy. Thirty years ago physicians were putting the sphygmograph aside as "of no value for diagnosis;" but, as I have said, physicians were then too much ruled by the statical conceptions of the deadhouse. They demanded of the sphygmograph that which it cannot directly indicate, namely, the site, form, or even the very existence of particular local lesions in the heart. But Mahomed, Sanderson, Galabin, and others—to speak only of English physicians—testified even then to its capacity of exhibiting, within limits, the dynamical conditions of the circulation, the kind and distribution of work done, which, after all, is the chief care of the physician. And how imperfectly we had availed ourselves of this capacity of the instrument we may learn from the remarkable treatise on 'The Pulse,' published but a few months ago by Dr. James Mackenzie. Unfortunately the sphygmograph, valuable as it is, when handled by those who are well aware of its limits, in the record of modes, forms, and distributions of pressure, cannot measure positive pressures. For many years, therefore, until lately when pressure gauges or sphygmometers of some trustworthiness were put into our hands,<sup>1</sup> I have had to compare arterial pressures as best I could with the practised and attentive finger; and to go without units and records. Thus, unsupported by permanent numerical computations, I have found it a difficult task to convince my brethren of the importance even of approximate estimates.

Arterial pressures vary very greatly. If I lift a chair from the ground my arterial pressure may rise 20 per

<sup>1</sup> My own observations were taken with von Basch's instrument and Hill and Barnard's; I have obtained better results with the latter instrument: Dr. Oliver's sphygmometer is well spoken of, but as yet I have no experience of it. It has seemed to me better to keep to one and the same instrument. Von Basch's instrument, or at any rate that one which I possess, registers 20 mm. Hg. above H. and B.'s, and thus I have been led occasionally to make false entries in my notes.

cent., and fall again as rapidly as I come to rest. During the use of the sphygmometer, if the patient be not cautioned against contracting his muscles—if, for instance, he be seated in a cramped position,—the pressure may fluctuate widely. On a certain occasion I observed a very high pressure rate in a patient in whom a high rate was not anticipated. No fault was found in the parts or arrangements of the instrument, and a second inflation revealed a still exorbitant though a lower rate; a third but a few minutes later registered an ordinary rate of about 120 mm. Hg., and remained steady about this figure. The previous excess I should still have attributed to some experimental fallacy, had not the patient, as I put the instrument aside, said to me that he had feared from it a violent electric shock; such as one which many years before, at a fair, had put him in an agony which he had never forgotten. As the shock did not occur he was reassured, and the pressure fell; perhaps some muscular area was tense, and thus relaxed. In patients who enter upon a consultation with acute anxiety of mind the pressure at first is often excessive. When close accuracy is of importance, then, it is well to take two observations,—one as the patient undresses; another, after all other physical examination, before he puts on his coat. The large majority of my observations are taken upon the patient seated easily at my table; it is better to keep to a uniform method, and in private practice this position is more convenient than recumbency. Observations on patients in bed run rather lower, but in my practice they have been comparatively few.

With Hill and Barnard's sphygmometer the pressures of adults vary from 95 (or even 90) to 105 mm. Hg., in temperate young men much occupied with athletic exercises to 250 mm. Hg. (the highest figure in the scale) in disease,—as, for example, in Bright's disease.<sup>1</sup> Between these

<sup>1</sup> On the day when these words were written I found maximum pressures of 230—250 in a man aged 65, whose arteries were yet fairly healthy, and in whom were no symptoms of renal disease. He com-

extremes every degree of variation may be found. I often apply the instrument in cases of life insurance, and in healthy men in middle life it should not record more than 120 mm. Hg. I have never applied it to a healthy woman, nor to a child.

In sufferers from arterio-sclerosis—I use the name arterio-sclerosis loosely for present convenience—exorbitant pressures are often, but by no means constantly found. Between disease of the arterial tree and blood-pressure there is no direct relation; in arterial disease, even in the extreme degree of it, normal or relatively low pressures are commonly observed; but I often notice that in cases of arterial degeneration the reading extends uniformly over a wider range of the scale—say over 15 or 20 units, in which cases I record the mean figure and the extreme. In denying that elevation of blood-pressure depends directly upon arterio-sclerosis I have stood alone for some years, against the high authority of von Basch and many others; but I note that some recent observers now admit the validity of my contradiction, and the matter is one of cardinal importance. So far as intermittent observations are to be trusted, I repeat that pressure may be, and often is, low throughout the course of arterial degeneration; or, again, having been high it may fall: though in some elderly persons with arterial decay occasional transient attacks of high pressure, such as occur at times in all of us, may be observed. I need scarcely add that a considerable and persistent fall late in a case, a fall not the result of treatment, and not coincident with general amelioration, usually signifies heart failure, and presages death within a few months; for it is remarkable how long high pressures are maintained, even when the dilated and overwrought heart is labouring towards the end of its day. When the subject of arterio-sclerosis begins to be

plained of slight vertiginous attacks, lassitude, and some loss of flesh. In a recent article in the 'Practitioner' I find that, by an oversight, a substitution of v. Besch's figures for Hill and Barnard's recorded a higher estimate of the low pressures of athletic young men.

short of breath he has entered upon the last stage of his pilgrimage.

If, then, arterial degeneration be a *vera causa* of elevation of blood-pressure, its effects may be and often are so modified by incidental and co-operative conditions as to be negligible. In many cases of arterio-sclerosis in which the blood-pressures are not high, to the best of our knowledge they had never been high. Conversely, however, high blood-pressures cannot long continue without straining the vessels; and I suggest that in elderly persons, in whom taint of lead, of syphilis, of alcohol, or other alien infection is set aside, and kidney disease also excluded, arterio-sclerosis be divided into two kinds; one the result of persistent high blood-pressure, the other the result of some more intimate causes, perhaps some unknown poison, or the tooth of time. It is very difficult in arterial diseases to find distinctive histological marks of kind, even in a kind so distinct as the syphilitic; the characters seem to depend more upon the rate than upon the kind of the change; but I think that what I am wont, speaking clinically of the radial and brachial, to call the "leathery" vessel, is suggestive of prolonged high pressure, persistent or past. The leathery vessel occurs in two aspects; as the narrow wiry artery more characteristic of the spare sallow subject, and the voluminous vessel common in the portly and rubicund. The quality of the arterial coats is more easily felt in the brachial artery, on semi-flexion of the elbow.

The leathery artery sometimes becomes calcareous, or is associated with calcified vessels elsewhere,—as, for example, in the brain; but when calcification is a prominent and comparatively early feature in the superficial arteries, pressures are apt to be moderate, or even low. In the so-called "ipecacuanha" radial high blood-pressure is by no means the rule; and, as high pressure is not the rule in these cases, so apoplexy is not the ruling event of them. Old persons with very calcareous and often grotesquely tortuous arteries, but with low pressures, are to be found

abundantly in every workhouse or asylum where the output of work is nominal and the diet spare. They live long, and die of an atrophy. Thus softening of the brain, and gradual or rapid vascular obstructions occur in the group; but cerebral hæmorrhage may be called rare in them. If the calcareous deposit lie in the tunica media the tendency of arteries would be to yield. In the wealthier classes these patients are found rather among the women, who are less addicted to high living.

Under conditions of high arterial pressure, on the other hand, of whatsoever causation, I need not say that apoplexy is frequent; apoplexy, uræmia, and outworn heart account for the end of most of them. Yet it has been a matter of surprise to me to see that very high pressure may be maintained, as it would seem, even for years, without much more apparent deterioration to the arterial tree than time of life might account for. I come here to-night, however, to urge an earlier recognition of such rising pressures, and the timely use of therapeutical means which shall prevent the strain and break-up of the circulating system. Herein, however, is the difficulty, that the subject of high pressure may not soon feel ill. Nay, a steady maintenance of high pressure in the brain may conduce for a while to a sense of vivacity and endurance. The heart has grown up to the work; and let me repeat my opinion, though now necessarily without argument, that the arteries hypertrophy likewise in the muscular coat, so that until these compensating growths in heart and artery dwindle or deteriorate, usually after the fibroid form, the patient may believe all to be well with him, and may not seek the physician till considerable mischief is done. Not infrequently, however, such persons come before us in an early stage of rising pressure, by the chance of some intercurrent disorder, or the prompting of some vague discomforts, such as a sense of fatigue and low spirits.

Let us take such a case, say in a patient of fifty years of age, a professional man, perhaps, a merchant, or a

student, who lives a sedentary life but lives well; for mental work and business cares create a desire even for more and richer food than bodily exercise in the fresh air excites, though they do far less for excretion. His sleep becomes disturbed, sick headaches are more frequent, he may be moody in rising from bed, and fretful and apprehensive until he warms to the day's work; a good luncheon and a glass or two of sherry improve matters, and in the evening he dines out cheerfully, denying himself nothing of meat or drink. We may tell him his liver is out of order, we may change his wine to whisky and soda, exhibit mercurials and salines, and send him to one of the spas; or we may do worse, we may not dwell on the laboured quality of the pulse, we may listen to the cuckoo cry of overwork, his wife will implore us not to lower him, urging that he is always better for his wine, and that a tonic and some rest are all that is needful; and too often he gets the tonic, and is sent off for six weeks' holiday, wherein to do as he pleases. In order to gain strength he indulges his appetite, but, as he does not dine out and gets plenty of air and exercise, he comes home better; yet only to repeat the same experiences nine months later, and to prescribe a holiday for himself, perhaps without consulting his physician. So he goes on, until one day he has a hitch in his speech, a cloud of albumen is found in his scanty and lateritious urine, and a trace of œdema upon his shins; his pulse is tighter than ever, his arteries are stretched like an old glove, and his heart is big and clanging. Partially remediable his state may still be, he may live for a year or two, but he is past cure. At one time I busied myself with deobstruents, rigid diet, and regulated exercise, to turn such a patient back into health; but, even in earlier stages than this, I was forced to realise that in the corporeal as in the moral sphere repentance may come too late. We may succeed more or less in our immediate purpose; the pulse does become softer under the finger, perhaps much softer; the heart comes in a little, the apoplexy or the pulmonary



congestion is staved off; but the patient pettishly persists that he is no better. And he is right; the stroke of death may have been parried, but what of that to a man who is good for nothing? Such a case, perhaps you will say, was a bad one; then I will dwell upon a man not so old, not yet incapable of some hard work, one whose deteriorated cardio-vascular state is apparent only to the skilled observer, but whose blood-pressure for two or three years has been 150—180 mm. Hg., and whose vascular system has thereby become stretched and inelastic; even in him treatment now can be but a compromise. If you bring his blood-pressure down to the normal you will make him slack and spiritless; his circulation has become adapted to an abnormal capacity, and you have henceforth to steer him as you can between the listlessness and malaise due to a reduction of pressure below his acquired habit on the one hand, and an apoplexy on the other. This is a task of much nicety and vigilance; and it is as likely as not that meanwhile the patient, who cannot enter into your refinements, will desert you for some more thoroughgoing practitioner.

But now let me suppose that the finger, educated by the discipline of the sphygmometer, leads us to suspect an abnormally high blood-pressure, and that we by the machine verify this in the first stage of the perversion,—that is, during the initial disorder of which I spoke. In this period no cases lend themselves more satisfactorily not only to palliation, not only to temporary amendment, but even to permanent cure. If excessive pressure be recognised in its earliest phases the course is clear, the treatment is not difficult, cure is fairly certain; and, with due watchfulness in years to come, shipwreck may be wholly averted. I cannot, then, urge too strongly the perils of neglecting these incipient increases of blood-pressure, and the importance of educating the finger in the early detection of them. Unfortunately in this incipient stage very few physicians are alert to detect this process, so baneful in its ascendancy but, if withstood in

its first manifestations, so fugitive ; for, unless the case be one of Bright's disease, we are too apt to be indifferent to some excess of pressure, and early cardiac hypertrophy is not easy to recognise. Nay, I have often heard patient and physician congratulate each other that at any rate the pulse is a good strong one. I am ready to admit that high pressure in the radial is not always unmistakable even to the vigilant touch ; although the aortic slap may be loud and the heart's apex a trifle outward. Often the pressure gauge is needed to convince us that the heart is thrusting against abnormal resistance. In the small hard pulse the hardness may escape notice in the small size of the vessel, especially if the wrist be fat ; moreover these contracted vessels do not so readily become tortuous : indeed, when the artery is larger and laxer, and the coat thickened, it is often difficult to be sure of excessive pressure, even when recourse to the pressure gauge, which must always be used in case of doubt, may prove it to be far above the normal. The reason of this latency of excessive pressure to the touch is a little difficult to understand ; fortunately the fallacy is more common in later stages when other features have become obvious. The sense of duration of the wave is often a better indication than that of tightness of the vessel.

Let us now return to the physics of the circulation. It is usually said—as, for example, by Sir Lauder Brunton but a few months ago—that “ arteries which lose their elasticity in old age offer an increased resistance to the blood-stream, and as a result the heart hypertrophies ; ” this eminent observer holding, I presume, the current opinion, which I have already challenged, that arterial disease comes first, and rise of blood-pressure consequently. Now I have always been ready to admit that the more carefully the principles of physics are studied in respect of living beings, the more apparent becomes the difficulty of calculating their validity under the complexities and contingencies which in biological problems

overlie and qualify them ; but we may feel pretty sure that resistance must depend substantially upon, first, the calibre of the tubes ; secondly, the viscosity of the blood. Is it, then, certain that defect of elasticity narrows the bed of the blood-stream as a whole ? Is it not at least as likely that, on the whole, it may widen it ? If in some areas an obliterative process prevail, in others distension may make up for it ; and the mean capacity of the channels at any rate may not be diminished.<sup>1</sup> Clinical observation of the cases of extreme arterial degradation without rise of pressure, to which I have already referred, impress this opinion upon me. If any chronic arterial disease narrows the bed of the circulating blood, surely it is the syphilitic. Now this manifestation of syphilis often occurs in young, active, and temperate men, and in many of these arterial pressure does not rise, as I have had occasion to ascertain in two or three cases observed continuously for many years—in one case for the last nineteen years of the patient's life, beginning at thirty-one, and ending with death by aneurysm of the aorta at fifty. In him cerebral symptoms had been distinct ten years before his death, and were wholly removed, though every superficial artery was thick. In another case of Jacksonian epilepsy due to syphilitic arterial disease the blood-pressure was normal during years of occasional observations ; and so on of many other such cases.

Omitting, then, the rarer arterial diseases, such as obliterative arteritis, neuritic arteritis, and periarteritis nodosa, I suggest three classes of so-called "arterio-sclerosis :"

(1) The involutionary—common in old people, often hereditary, not necessarily or usually associated with rise of arterial pressure ; the nature of which, intrinsic or extrinsic, is unknown, but does not lie in high living.

<sup>1</sup> I cannot at present discuss a permanent arteriolar contraction attributed to irritating blood ; but I am not omitting a very important factor, as accumulations of blood in the splanchnic area should neutralise the arterial stress.

This kind may be vaguely referred to the "faltering rheums of age."

(2) The mechanical—the result of long-persisting high blood-pressure of whatsoever origin.

(3) The toxic—resulting from such causes as lead, alcohol, or syphilis ; usually met with in younger persons, in some of which cases the pressure rises, in others not.

I must now undertake the formidable task of meeting in the gate those many opponents who will tell me that the cases of rising arterial pressure I have cited are virtually if not obviously cases of granular kidney ; or at least to notice for a moment the current phrase, "renal inadequacy." This equivocal phrase, introduced by Sir Andrew Clark in—I venture to think—one of the less successful essays of this sagacious physician, suggests notions founded, as yet at any rate, on no positive facts or reasons, and lends itself too readily on the one hand to those hollow explanations which are a snare to us, and on the other to the inexorable dictations of the dead-house. Professor Osler tells us he is satisfied that arterio-sclerosis is not essentially connected with granular kidney. In a recent thesis of considerable merit one of my graduates tried to convince me of the secret influence of granular kidney in arterial disease by collecting the records of a vast number of necropsies of the kind, and declaring the existence of fibroid changes in the kidneys in 94 per cent. of them. A large part of his list consisted of cases of elderly and even aged persons in whom no definite diagnosis of Bright's disease had been made, but in whose dead kidneys a greater or less amount of fibroid deterioration had been detected. The list contained also of course a large number of cases of granular kidney properly so called, with which cardiac arterial disease was as usual associated ; with these last we have now no further concern.

It is impossible at this hour to enter upon the pathology of the fibroid deteriorations found in the kidneys no

less than in many or most other organs of old subjects ; but I must briefly indicate my opinion that this process has little or nothing in common with that of granular kidney proper. This fibroid deterioration is a partial atrophy or a factor of an atrophy, and is consistent and generally associated with a large remnant of normally secreting elements. Granular kidney, on the contrary, is the result of a protracted exposure of the whole kidney to the action of some poison, often unknown, which had primarily a necrosing effect on the secreting elements. This effect is best seen in the acuter cases, as in the kidney of pregnancy, of typhoid fever, of diphtheria, and the like, where the poison is more virulent, the corrosion more acute, and the results less obscured by the attempts at repair by which in slower and less virulent invasions corrupt parts are removed and the living remnant is shored up.

And I must appeal again from the deadhouse to clinical observation : chronic Bright's disease is a malady with features of its own, and has its mean incidence at a somewhat earlier age than the malady I am discussing. Among these features are undoubtedly high arterial pressure, and the baneful consequences of cardio-arterial strain ; but leaving aside for the moment the quality of the blood, the state of the retina, and other characteristic symptoms, a careful supervision of the urine alone will distinguish Bright's disease, if, in some obscure cases, not on a single interview, yet certainly after some days' vigilance. I am not concerned to confine myself to well-marked Bright's disease ; I am ready to assume that the process, especially in the elderly, may be so chronic as to present its symptoms in a larval shape ; yet even in cases so slow, so insidious, a careful study of the urine will tell us if the case turns upon the kidneys. In the kidneys of old persons undergoing involutionary change, there is secreting area enough to clear the system. Dr. Rose Bradford's ablation experiments support our experience herein ; and histological methods rarely exhibit in these cases a deep

intrusion of alien tissue. Physicians who allege renal inadequacy must do what they have not done, namely, produce, let us say, at least a week's urine, duly tested by chemical and microscopical methods. Every day the whole of the urine must be collected (the patient being sent to the chamber-pot before every visit to the closet), and the solid contents of each day's issue registered. If the disease turn upon the kidneys, the solid excretions, taken say for seven to ten days, will be far below the normal mean for the given diet. Moreover, with proper precautions, casts will often be found, and albumen, at times abundant, will rarely prove to be absent for many days together. Even in the early stages of disease we may distinguish the high arterial pressure of renal origin from that not of renal origin, as in the latter albumen is absent, but in the former if not constantly is frequently present. Granular casts, again, absent in the non-renal cases, in the renal are not infrequent. Such a case as the following is no uncommon one. A man between fifty and sixty years of age presents himself with a big heart, thick and tortuous arteries, a blood-pressure of 230 to 240 mm. Hg., and some œdema of the lungs. Death may be staved off for a while, but his condition is perilous. Now, if ever, his urine should present evidences of "renal inadequacy." He passes for us, however, a small quantity, high in colour, of normal or high specific gravity, which thickens as it cools, and may paint the bottom of the pot. There may or may not be a little albumen in it; but, even after spinning, no casts or but a few hyaline casts are discovered. On subsequent observation during alterative treatment, a week's urine proves to be up to the normal mean of solid excretion, or the fall in urea corresponds with a restriction of the diet, a condition often forgotten. After death we find the kidneys tough, the capsule a little adherent, the surface a little rough, and presenting some shallow intrusion of fibre into the parenchyma; and we find evidences of fibroid deterioration not only

in heart and arteries, but in many other parts also. Now, Sir, I have watched such cases from beginning to end for many years, and in not a few of them I have witnessed all the phases of the malady in the same individual: the lesson I have learned from them and would impress upon others is that the first deviation from health is not arterial disease but rise of blood-pressure, the arterial disease being secondary and due to strain; that, although this malady has in common with Bright's disease the feature of a rise of blood-pressure and consequent cardio-arterial strain, and possibly some affinity of causation, it is essentially distinct from the latter, and has no tendency to drift into it; that on its first appearance this arterial plethora is remediable; nay, on its second or even third appearance it may be driven away; and that even when somewhat advanced, if the tendency may not be eradicated, it may under due regulation of life and medicine be held in check.

On the causes of the process I have described I have little to say worth your hearing. If you call it gouty you will give me little help. Gout is a clinical series, in the type of which inflammation of a joint or joints must be included, and in which rise of arterial pressure is not the rule, or if present is incidental. I find that in many men badly afflicted by recurrent gout, if free from kidney disease and of temperate habits, rise of arterial pressure does not occur; their vessels remain fairly healthy, and they attain to ripeness of years. Persons accused of "suppressed gout" are found in every consulting room; their only common feature seems to be the absence of the chief characteristic of gout, namely arthritis; they solicit it, they pray for it—for they believe it would resolve their disorders: but they pray in vain. On the nature of overt gout he is a bold man who expresses a positive opinion; suppressed gout I believe to be the label of a heterogeneous bundle of maladies, many of which have little or nothing in common: but among them my arterial plethora plays a large part. That this malady has any part in

gout, or gout any part in it, I have no knowledge or surmise: their association in the individual seems to me not to exceed the ratio of mere coincidence, though gout seems to have more than this ratio in the family history of such patients. Arterial plethora is not a common disease in the poor; nor in persons who live actively, and eat and drink sparingly.

And this brings me to the second physical factor of blood-pressure, namely, the viscosity of the blood. For nearly ten years past I have endeavoured, but with much mishap, to estimate this factor. I ought to have taken it up myself, but have hoped to get it worked out by some of my pupils. Time after time the subject has been agreed upon for a graduation thesis, and as often the research has broken down for one reason or another. My suggestion is that, in the simple cases of rising arterial pressure I am discussing, the blood is above the normal viscosity; it will not be difficult to ascertain this, and I expect very soon to have some definite results to offer. Dr. Haig assures me that in gout the blood does stick in the finer vessels, and because of admixture of uric acid; and he most kindly sent to me a little instrument by which this lagging is to be demonstrated, an instrument of which as yet I have had insufficient experience. Dr. Gowland Hopkins tells me that the experiment of injecting uric acid or purin bodies into the circulation of animals during the observation of blood-pressures has never been made. That we have to do with some of the purin bodies, lately investigated by Dr. Walker Hall and others, is highly probable; that uric acid is the offending element I have not satisfied myself. In some persons it may be that faulty metabolism, without extrinsic poison, may set up granular kidney; and my observation that under mental distress a fault of this kind is apt to arise, and to have this issue, is, I think, now generally admitted to be true: in other persons some such perversion, sparing the kidney, seems, primarily and of itself, to set up resistance in the periphery of the circulation, and thus to



lead to strain of the arterial tree. It may be that the formation of "anti-substances" to protect the system against the toxins of metabolism is not equally active in all persons. The disposition to fibrosis, which is found generally, if not universally, in the tissues of such a patient, may be a direct consequence of the perverted juices, or may be a feature of slow atrophy due to failing blood-streams. The *vasa vasorum* suffer early, and it is as yet impossible to say what part, whether as cause or consequence, these tiny channels play in the deterioration of the larger vessels which they should nourish. Of these *vasa vasorum* the coronary arteries are the chief; here, however, we see to our surprise—as I urged more at length in my Lane Lectures of 1895 and elsewhere—that the heart can hypertrophy, and in substantial measure of time and degree retain its hypertrophy, when its coronary arteries are both of them occluded.

On treatment I can now touch only in the briefest way. If, as I believe, one main cause of rising arterial pressure in middle life is excess of feeding,—that is to say, of food in excess of work and excretion, the remedy obviously lies in prevention. That alcohol, apart from excess of food, will produce the condition I am not sure; I think not: on the other hand, I do feel sure that with such excess it is a potent ally; as in its alliance with arsenic, it seems to prepare the way by lowering tissue resistance. We see a few old men who, usually of lean habit and inheriting longevity, are endowed with enormous and persistent energy of mind and body, who have never denied themselves meat or drink, but yet at threescore and ten or fourscore years have good arteries and a moderate blood-pressure; but such men are few: in most persons, as life slows down, the powers of expenditure and excretion fall within much narrower limits. The ordinary man must be warned, say as he passes the age of forty, to keep up muscular exercise in the fresh air, and to control his appetite. Many, I should say most, men eat and drink far more than they need for the day's work.

They are supplied generously with food, without hunting for it; and annual bloodletting has gone out of fashion. As soon as high pressure becomes manifest, rigorous diet, deobstruent remedies, and exercise in the open air, such as cautious hill climbing under the careful regulation of the physician, are necessary; and necessary not only during a Homburg month and its "after cure," but also for the rest of the patient's life. Catch him early, and he is quite curable; let him drift, and cure may be out of reach.

My purpose to-day is fulfilled if I can impress upon my hearers the importance "*obstare principis*." It is in such means as these that we see the value of the Chinese practice of paying the physician only during the days of health, though the method should be supplemented by a provision for the recovery of damages from the patient who disobeys our prescriptions.

## DISCUSSION

Sir WILLIAM BROADBENT found himself in general agreement with practically every point of importance in the paper. It was desirable to have a clear idea of what was meant by rise of blood-pressure in later life. Professor Allbutt had referred to the marked effect of emotion in causing a rise of blood-pressure, and there were many other conditions which temporarily produced a similar result. The estimation by any instrument of the blood-pressure at the wrist or elbow meant the gauging of the force of the heart's contraction. The rise, in later life, was due to more ; its worst effects might develop when the heart was not capable of giving high records. The more important cause was peripheral obstruction. The one rise was fugitive, the other permanent. The obstruction arose either in the arterioles or in the capillaries, probably in the latter, as suggested by the miliary aneurysms in the minute arterioles, indicating obstruction in the capillaries beyond. The degree of pressure in the artery and the fulness of the vessel between the beats were the two indications. The condition was sometimes recognisable in the child, the schoolboy, and often in men under thirty. Small arteries did not, in his experience, occur mostly in spare individuals. The connection between high blood-pressure and kidney disease was indirect ; in many cases there was no such disease ; it was probably due to a blood condition which also gave rise to the renal disease, and this, when established, was itself an accessory cause, since toxic substances were not removed by the kidneys from the blood. Renal inadequacy had nothing to do with high arterial tension. As to the ultimate consequences of the condition, the causation of heart defects was important. The heart frequently gave way before the vessels, as in acute cardiac dilatation. The whole of the changes in heart and vessels were secondary to the increased peripheral resistance. Long ago he had brought forward evidence that the high blood-pressure of renal disease was due to active contraction of the muscle of the vessel walls as shown by the immediate effect of nitro-glycerine, and that that, due to a blood-state. In advanced life there were arterial changes with which high blood-pressure had nothing to do, and without any cardiac changes. The more common brain result of this was thrombosis and cerebral softening. Syphilitic arterial disease affecting both the large and small arteries gave rise quite commonly to aneurysm independently of any high arterial tension, and aneurysm was very rare in renal disease, and in cases of high arterial tension which were independent of syphilis.

Dr. ALEXANDER HAIG said that eight years ago he had made

experiments of injecting uric acid into animals, but the results had always been negative and were not published. From fifteen to twenty grains of uric acid were injected into animals while manometric observations were being taken, and then the whole of the blood was collected. When the uric acid was estimated in this it was found that there was no increase over the amount normally present. The probable explanation of this fact was that the uric acid which had been injected was probably taken up by the liver. He stated that the return of circulation in the skin, after pressure, was twice as slow in a person on meat diet, or in one who had ingested uric acid, as it was in a person on a vegetable diet, and this fact showed that there was a contraction of the finer vessels.

Dr. NEWTON PITT thought the younger school of pathologists would agree that high arterial tension was the predecessor rather than the sequel of vascular disease. Reference was made to observations by Dr. Herbert French to the effect that in chronic Bright's disease there was no retention of nitrogenous products in the blood, the amount of nitrogen in the ingesta and excreta being practically equal, and similar observations were recently advanced at the Cairo Congress. It would seem, therefore, that the vascular degeneration could not be due to an increased amount of nitrogenous products in the blood. The smallest amount of retention daily would speedily lead to a conspicuous increase and a speedy death.

Dr. H. D. ROLLESTON said that among the interesting questions raised by Professor Allbutt two were especially important. Firstly, the relation of high blood-pressure to arterio-sclerosis, which had already been fully dealt with; and secondly, the relation of kidney disease to arterial disease. No doubt tubal nephritis might lead to increased blood-pressure, and so to degeneration of the muscular coat and the compensatory process of chronic endarteritis. The gradual alteration of a large white kidney into a small white kidney was due to arterio-sclerotic changes in the vessels, which diminished the blood-supply to certain portions of the kidney substance, and fibrosis resulted in those portions from which the blood-supply had been cut off. The nitrogenous excretion and intake was not the whole matter; other toxic substances might be retained in the body, causing vascular spasm and arterial degeneration with the action and reaction of the kidneys on the circulatory organ. Chronic granular kidney was probably a multiple fibro-substitution process. An ordinary granular kidney was rather a mechanical effect of arterio-sclerosis depending on impaired blood-supply than an inflammatory process. Imperfect renal secretion might give rise to high tension and compensatory arterial changes.

Professor ALLBUTT, in reply, held that there were certainly two factors in high tension—a proportional heart vigour to an

increased peripheral resistance. The heart usually gave way by muscle or valve failure if apoplexy had not previously occurred. The maximum pressure of aortic regurgitation was very high, but the minimum was very low; he had been referring to mean blood-pressures. High tension was a phrase which he thought could only be applied to a dead tube, not to a living artery. The corresponding changes in children in blood-pressure and uric acid excretion were episodic, and possibly due to an infection. There were many causes of high blood-pressure. Observations on the viscosity of the blood were required; it must be the immediate cause of the peripheral resistance. The specific gravity was another matter. In nephritis the principal thing was a toxic process injuring the renal epithelium; an inflammatory reaction was not essential.



# SUPRA-PUBIC CYSTOTOMY IN CASES OF TUMOUR OF THE BLADDER

WITH SPECIAL REFERENCE TO THE CAUSES OF  
MORTALITY AND OF RECURRENCE OF  
THE GROWTH

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SUPRA-PUBIC cystotomy in cases of tumour of the bladder has hitherto been almost the rarest abdominal operation in the practice of general surgeons. Since 1894<sup>1</sup> I have only performed the operation seven times, with one fatal result. But this statement by itself would give an erroneous idea of the mortality which has attended my operations. I can recall two antecedent ones at the Great Northern Central Hospital which both ended fatally. One of the patients was an old man whose bladder was explored,

<sup>1</sup> The date is given because I possess no proper notes before the year 1894.

and found to contain a huge sloughing epithelioma; he died of pelvic cellulitis. The other was a woman who had two papillomata removed, and afterwards died of shock and suppression of urine. Thus out of nine operation cases I have lost three. Presently the cause of this high mortality will be discussed, and then it will be seen that it is by no means exceptional for this class of case. The fate of the survivors was far from satisfactory. In the first the carcinoma was so extensive that I could not attempt its removal. In the second the extraction of a quantity of innocent papilloma was followed by suppression of urine and by a dangerous illness. In the third the pelvic lymphatic glands were felt enlarged during the course of the operation. The patient died thirteen weeks after the date of the operation from nephritis. (Operation April 29th, 1897; died August 9th, 1897.) In the fourth a papilloma was removed by forceps and elastic ligature on February 11th, 1899, and a small recurrence was seen with the endoscope on February 6th, 1902. In the fifth the papilloma was small and incrustated with phosphates. It was erased and burnt. Since her recovery she has had a child, and is now quite well with normal urine. (Seen February, 1902; date of operation November 25th, 1899.) Lastly, in the sixth a papilloma was seen with the endoscope at the mouth of the left ureter. When the bladder was opened the growth was found to have hidden an ulcer of the mouth of the ureter. On December 8th, 1900, the growth was removed and the ulcer cauterised. A year afterwards my friend Mr. John Gay told me that although the patient was better, yet he occasionally had attacks of hæmaturia. Hereafter I propose to refer to these cases, because they throw light upon the cause of the high mortality, and also of recurrence of the growth. In addition they illustrate points in the methods of operating. Their number is, however, far too small to justify any general conclusions, and therefore I have abstracted the notes of supra-pubic cystotomy in cases of tumour of the bladder from the Clinical Records



of St. Bartholomew's Hospital from the year 1891 to 1900 inclusive.<sup>1</sup> During this decade fifty-three operations were performed upon thirty-seven patients. Of these thirty-two patients had one operation, two had two, two had four, and one had nine.

At the outset I propose to scrutinise the clinical material, to see what light it throws upon the question of mortality. This may be calculated either upon the number of *patients* or upon the number of *operations*. It is obviously of great importance not to confuse the two methods. If we take first the thirty-seven patients upon whom supra-pubic cystotomy was performed for tumour of the bladder we find that twelve died and twenty-five recovered. Until these figures were seen I thought that the high mortality which had attended my own operations was exceptional.<sup>2</sup> If we now calculate the mortality upon the total number of *operations* a more favourable result is obtained. Fifty-three operations were followed by twelve deaths and forty-one recoveries. The improvement in results is, of course, due to the recoveries of those patients who had repeated operations performed for the removal of papillomata. One man was operated on for the ninth time, two others for the fourth, and two patients who were operated upon twice; both died after the second operation.<sup>3</sup>

<sup>1</sup> It is to be observed that the statistics of the Surgical Registrar are based upon the number of operations, and not upon the number of patients. Also that under the head of supra-pubic cystotomy cases of tubercle are sometimes included. I have not included amongst operations such procedures as those in which a supra-pubic wound was merely reopened before it had healed in order that the bladder might be explored, or pieces of tumour removed. In addition I have eliminated cases in which the growth was entirely prostatic. In the St. Bartholomew's cases are included four of my own, which all recovered. In addition I have included a case in which the tumour was found to consist of a cancerous middle lobe of the prostate projecting into the bladder. It could not be removed, and the patient died.

<sup>2</sup> Such, however, is clearly not the case. Sir Henry Thompson, operating upon very severe cases by the perineal route, had six deaths in twenty patients ('Tumours of the Bladder,' 1884, p. 98, *et seq.*).

<sup>3</sup> It is probable that one of the patients who had four operations died

In searching for the causes of this high mortality it is simpler to begin with the thirty-two cases in which a single operation was performed. Sixteen of these had the bladder tumour removed in one way or another, and in sixteen the tumour could not be removed. Three of the first class died and seven of the second. In other words, one set of sixteen with removable tumours had a mortality of less than one fifth, and the other set of sixteen with irremovable tumours had a mortality of nearly one half. Such a striking difference suggests that in the last set some new and deadly complications must have arisen.

The causes of death in the three cases in which the tumour was removed were as follows:—A man, who had a carcinoma removed by clamping its pedicle with forceps, died of profuse and rapid hæmorrhage, followed by pelvic cellulitis; the urine was acid before the operation. Next, a man aged thirty-three died of shock after partial cystectomy for the removal of an epithelioma. The growth began an inch above the prostate, and reached three inches up the left side of the bladder. About one third of the bladder was excised, together with the end of the left ureter. The pelvic lymphatic glands contained secondary growth. His urine was acid before the operation. Lastly, a man aged fifty-eight had a papilloma removed from the left side of the base of the bladder. The stalk of the growth was transfixed and ligatured with silk. Death followed from pelvic suppuration, ascending pyelo-nephritis, and pyæmia. His urine was acid before the operation. Thus two of the three died of sepsis, the onset of which seems to have been at or after the operation.

after a fifth performed in the London Hospital. The fourth operation at St. Bartholomew's was abandoned. But Mr. E. H. Fenwick ('Operative and Inoperative Tumours of the Urinary Bladder,' London, 1901, p. 111), in describing one of his cases, writes as follows:—"A patient operated upon four times previously at St. Bartholomew's Hospital by Sir Thomas Smith, anæmic and in great distress from blockage by growth. Opened up a supra-pubic sinus, found large masses of villus-covered carcinoma springing from the posterior wall along the trigone, and encroaching on urethral orifice; free removal; packed with gauze. Did well at first, but died of exhaustion."

Of the seven cases which died after one operation and without having the tumour removed, one died of shock and hæmorrhage, three died of sepsis, and three were not examined after death. Of the three septic cases, one died of pelvic cellulitis, one died of suppurative peritonitis, and one of prostatic abscess and pelvic cellulitis.

It would be rash to surmise the cause of death in the three cases which were not examined. Pelvic cellulitis and septic peritonitis may both make considerable progress without their presence being suspected. This is shown by one of those who died after a second operation. A year after the removal of the villous tumour the hæmaturia recurred, and was accompanied with rigors and high temperature. The patient died upon the fourth day after the removal of more villous growth, and extensive pelvic peritonitis was discovered. Its existence had not been suspected.<sup>1</sup> The other patient, who had a second operation performed, died of ascending pyelo-nephritis with pyonephrosis.<sup>2</sup>

Unfortunately it is useless to try and compare the cause of death in the cases in which the tumour was removed with those in which it was left, because the numbers are so small. But by adding to the three cases in which the tumour was removed six more in which it was not, we have nine cases in which the cause of death is known. Seven died of sepsis, one of shock, and one of shock and hæmorrhage. Clearly sepsis is the great danger of supra-pubic cystotomy in cases of tumour of the bladder; and after sepsis come shock and hæmorrhage, but they come a long way after.

I will now try to inquire how the sepsis occurs, and why it is so fatal. And first we may put aside the likelihood of bacteria being carried to the wound by the blood-stream. Auto-inoculation is possible, but not

<sup>1</sup> "Surgical Registrar's Notes," 'St. Bartholomew's Hospital Reports,' vol. xxxii, 1896, p. 160.

<sup>2</sup> The papilloma in this case was probably complicated by tubercle. It is stated that caseous deposit was found in both epididymes, and that one of the vesiculæ seminales was full of pus.

probable. The alternatives are, first, that the sepsis may be present in the genito-urinary tract at the time of operation; second, it may be introduced during the operation; and third, it may enter after the operation.

Unfortunately the clinical notes give no precise information upon these three alternatives; but, as a rule, they state whether the urine was acid or alkaline before the operation; whether cystitis had begun; whether the urine was mixed with pus or muco-pus; or the time when it became alkaline. It is well known that various kinds of bacteria may be present in the genito-urinary tract, although the urine which is passed is acid.<sup>1</sup> But in the class of case under consideration, although it is not safe to infer that acid urine betokens asepsis, nevertheless we may assume that pus, muco-pus, and alkalinity indicate sepsis.

If now we take again the patients who underwent one operation, and again divide them according to the removability or irremovability of the tumour, the results are as follows:—The condition of the urine is known in fourteen of the sixteen who had the tumour removed. In twelve the urine was acid, in two it was septic, but not in a high degree. Three of the twelve patients with acid urine died. I have already said that one died of shock; one of profuse and rapid hæmorrhage followed by pelvic cellulitis; and one of pyæmia following upon pelvic suppuration and ascending pyelo-nephritis. The two patients with septic urine both recovered. They were females, and, as it happens, were both under my own care. One had very slight sepsis, her papillomata being covered with a thin and recent deposit of phosphates. The other had an ulcerated and pedunculated epithelioma with a circumference of eleven inches. The sepsis was considerable, but I made determined efforts to disinfect the

<sup>1</sup> 'Cystitis und Urin-Infektion,' by Max Melchior, Berlin, 1897, p. 73, *et seq.* My colleague, Dr. F. W. Andrewes, recently reported that the urine from a case of cystitis was acid, and full of colon and other varieties of bacilli.

bladder. The condition of the urine is noted in thirteen of the sixteen patients with irremovable tumours. Three had acid urine and ten alkaline. A man with an irremovable ulcerated epithelioma had acid urine, but it contained pus and blood. He recovered from the operation, and all his urinary symptoms remained in abeyance for several months. A second patient with acid urine died of shock and hæmorrhage. The urine of the third patient was faintly acid before the operation. Death ensued from diarrhoea and hæmaturia. At the post-mortem examination suppuration was discovered in the psoas and iliacus muscles and in the pelvis, and the peritoneum was inflamed.

The remaining ten patients with irremovable tumours all had septic urine, and five of them died. As no post-mortem examination was made in two out of the five the cause of their death is unknown. Of the other three it is known that one died of suppurative peritonitis, one of cystitis, and one of extravasation of septic urine.

It may be remembered that two patients died after a second operation. One was septic before the second operation, and died of ascending pyelo-nephritis. The other had septic urine at the time of the second operation, and died of purulent peritonitis.

I shall not try to generalise from such a small number of cases; nevertheless I venture to point out one or two obvious conclusions. And, first, how much safer the operation of supra-pubic cystotomy is when the urine is acid and the tumour removable. Indeed, it seems reasonable to suppose that if shock and hæmorrhage could be prevented—and I believe that they could—the mortality would fall within very reasonable proportions.<sup>1</sup>

Second, the cases clearly show the extreme danger of

<sup>1</sup> Mr. E. H. Fenwick (*loc. cit.*, p. 103, Appendix B, "One Hundred and Thirty-five Removals of Growth from the Bladder," and of which he says, "I believe the list contains all the operations I have purposely performed for the relief of growth of the bladder up to the end of April, 1901") records nine deaths in the 135 cases. Mr. Fenwick most properly advocates careful selection and asepsis.

supra-pubic cystotomy when the urine is septic and the tumour irremovable. I have come to the conclusion that an operation is not justifiable under such circumstances. It is true that now and then a survivor experiences some relief from the horrors of the disease, but that relief is not worth attempting when the attempt entails a mortality of fifty per cent. Irremovable tumours of the bladder are almost invariably malignant. This was the case with fifteen out of sixteen under discussion, and it is almost certain that the sixteenth was also malignant. Now the ordinary course of malignant disease on any surface of the body is growth, degeneration, ulceration, and sepsis. In tumours of the bladder the growth is almost invariably accompanied by hæmorrhage, which may be fatal, but in any case predisposes to septic cystitis, and, indeed, to general sepsis. Further, the sepsis which complicates malignant disease is of a virulent type. Surgeons are well aware of its dangers. The only operation case I can remember to have lost from septicæmia had a foul and ulcerated carcinoma of the breast.<sup>1</sup> While operating upon malignant disease complicated by sepsis the freshly cut tissues are sure to be infected, and the infection easily enters the bloodstream. I do not believe that the sepsis which complicates malignant disease of the bladder is more virulent than that met with in malignant disease of other regions, but owing to the proximity of the ureters and kidneys, of the pelvic veins and cellular tissue, and of the peritoneum, it has unusual opportunities of doing harm.

Unfortunately, by far the largest proportion of bladder tumours are malignant. I have collated fifty-eight cases from the clinical records of St. Bartholomew's Hospital from the year 1891 to 1900 inclusive.

The diagnosis is based on information obtained by post-mortem examination, supra-pubic cystotomy, urethral dilatation, or clinical examination disclosing a growth in the bladder and secondary growths elsewhere. In many

<sup>1</sup> 'Hunterian Lectures on Traumatic Infection,' London and Edinburgh, 1896, p. 51.

instances the macroscopic was confirmed by microscopic examination. Thirty-six of the fifty-eight cases were malignant, and in four of these the growth also involved the prostate. Eight were doubtful, but more likely malignant than innocent. Fourteen were supposed to be innocent. Three of the latter were discovered accidentally at post-mortem examinations. Two out of the three died from the effects of accidents, and one of cancer of the œsophagus. This gives a proportion of about four malignant or doubtful to one innocent tumour. But it is possible that these statistics are too favourable. Albarran<sup>1</sup> examined eighty-eight tumours of the bladder with the microscope, and found that seventy-one of them were malignant and seventeen were innocent, a proportion of about five malignant to one innocent.

The discrepancy is probably capable of simple explanation. I think we may assume that a good many tumours with thin pedicles have been thought innocent, especially in the absence of a microscopical examination.<sup>2</sup> But it is now known that the thickness of the pedicle is not a reliable guide to the characters of the growth.<sup>3</sup> Perhaps the slender-stalked villous papillomata may be an exception, but even they are at times associated with malignant growth. The extreme frequency of malignancy in tumours of the bladder, and the fallacy which underlies the naked-eye appearances, have an important bearing upon the methods of treatment.

The high mortality which attends supra-pubic cystotomy in cases of tumour of the bladder can be greatly lessened. In my own small experience it has been mainly due to the violation of the general principles of surgery. It is now almost certain that two of my fatal cases ought not to

<sup>1</sup> 'Les Tumeurs de la Vessie,' Paris, 1892, p. 165.

<sup>2</sup> Albarran, loc. cit., p. 46.

<sup>3</sup> "There is a general belief, I think, that pedunculated growths are usually benign. This is a very dangerous belief" (Jacobson, 'The Operations of Surgery,' 3rd edition, p. 972). "I cannot say, however, that much can be learnt from the actual appearance of the villi as to the benign or malignant character of the growth" (Fenwick, loc. cit., p. 15).

have been attempted. In one a huge irremovable malignant growth was found, and it was complicated with sepsis. Now surgeons will agree that if a malignant growth cannot be entirely removed it ought to be left alone. Nothing can be more unsurgical than to perform an incomplete, futile operation, and at the same time expose the loose cellular tissue and veins of the pelvis, and the peritoneum to a virulent form of sepsis. In the second case the growth, although apparently innocent, was of at least twelve years' duration, filled the bladder, and was complicated with sepsis. The patient never rallied, and died on third day. It is probable that he had arrived at the stage of ascending pyelonephritis. My third fatality was due to shock.

Clearly, the proper time for operation is (1) before the growth is too extensive for removal and (2) before sepsis is established. Both of these requirements are fulfilled by an early diagnosis. This can in nearly every case be achieved. The growth would be seen if the bladder endoscope was systematically used after the occurrence of sudden spontaneous hæmaturia. Hæmaturia is the commonest and earliest symptom of bladder tumour. It was present in forty-three out of forty-five cases.<sup>1</sup> In the two in which it was supposed to be absent the urine was not examined with the microscope. In about one quarter of the forty-three cases the blood was accompanied with pain. In about three quarters the hæmaturia was preceded, accompanied, or followed by other symptoms, such as pain during and at the end of micturition, pain in the back, abdomen, rectum, vagina, root or end of penis, pubes, rectum, perinæum, and neck of bladder. Sometimes the hæmaturia was preceded by increased frequency of micturition, and sometimes was followed by retention or incontinence. Bits of growth were occasionally passed, or the urine contained suspicious epithelial cells. Unfortunately the first attack of hæmaturia soon subsides, and may not recur for months or even years, and the patient is

<sup>1</sup> 'St. Bartholomew's Hospital Clinical Records.'



supposed to have recovered. The absence of pain affords a false sense of security, and is an additional cause of delay in using the endoscope.

I do not propose to enter upon the details of the endoscopic examination. They are fully given in the writings of Harrison, Fenwick, Nitze, Posner, and many others. I would merely remark that when a tumour is seen and judged to be suitable for removal it is best performed forthwith. This not only avoids a second anæsthesia, but also diminishes the danger of sepsis and of hæmorrhage. But if, owing to hæmorrhage,<sup>1</sup> pus, enlargement of the prostate, or the presence of a quantity of growth, nothing can be seen, then it is certainly better to delay. After rest in bed the hæmorrhage may subside, and the pus may be diminished by washing out the bladder with solution of nitrate of silver. A growth felt above the pubes, or by the rectum, or by the vagina, cannot, as a rule, be removed. Small removable growths may, however, be sometimes felt *per vaginam*.

Although my own experience is so small, perhaps I may be allowed to refer very briefly to the details of the operation. In the first place, each step in the removal of the growth ought to be guided by the clearest vision. This requirement excludes the perinæal operation, and also those which in females are attempted *per urethram*. I have found five cases in the St. Bartholomew's records of the last decade in which the removal of the growth was attempted *per urethram*. One is called an exploration. The tumour was an ulcerated carcinoma, too extensive for removal. The woman died of pelvic cellulitis. The right ureter was blocked by a calculus, and the kidney small and full of pus. The lumbar lymphatic glands were the seat of secondary growth. In the second case the operation was followed by hæmorrhage and cystitis, and in ten weeks it was clear that the tumour had grown again. In

<sup>1</sup> I have found a mixture of tincture of hamamelis and boric acid lotion, 1 in 40 to 1 in 20, most useful in arresting hæmorrhage from the growth.

the third a severe hæmorrhage occurred seven weeks after the attempt at removal. In the fourth a malignant growth was partially scraped, and afterwards a catheter had to be used. Finally, in the fifth the growth had a thin pedicle and was removed with forceps; the patient was well three months afterwards. It is clear that this is the only one of the five which had much chance of being cured.

I think it will be allowed that for exact vision a full-sized supra-pubic opening is required, aided by efficient retraction of the edges of the wound and by the use of an electric forehead lamp.<sup>1</sup> It is unnecessary to discuss this step in the operation. Hitherto I have used strong silk threads as retractors. After the bladder has been opened by a vertical incision one or two threads are passed through the walls of the bladder and of the abdomen on each side of the wound. Besides serving as retractors they prevent the bladder falling back. There is, however, much difference of opinion as to the best mode of retraction. A glass vaginal speculum may, as Mr. Fenwick has suggested, prove of great service in bringing the tumour into view. Next as regards the removal of the tumour. Owing to the fear of hæmorrhage a great variety of clamps, ligatures, and cauteries have been tried at St. Bartholomew's. These have been combined with scraping and excision of the projecting part of the growth. I cannot tell with certainty what proportion of these tumours continued to grow. In one of them I put a clamp upon the pedicle and then an elastic ligature beyond the clamp. Three years afterwards a growth was seen with the endoscope at the spot whence the former was supposed to have been removed. In at least seven others the tumour grew again, or, to speak more correctly, continued to grow. In some of these repeated operations had to be performed. Thus out of twenty patients who recovered from so-called removal of the growth, eight were known to have relapsed.<sup>2</sup>

<sup>1</sup> I think it is better not to use Patersen's bag, because its introduction increases the danger of sepsis.

<sup>2</sup> This does not include those attempted *per urethram*.

If we assume that the remaining twelve had all been cured (which is quite improbable)<sup>1</sup> the results would still be unsatisfactory.

I have already pointed out that the proportion of malignant growths to innocent was four malignant to one innocent. Some would accept this as a sufficient explanation of the recurrences. But it is recognised that malignant growths of the bladder do not possess a high degree of malignancy. Their growth is slow; they take a long time to penetrate the walls of the bladder; they only invade the lymphatic glands in their later stages; and secondary growths in the liver and other organs are by no means common. On the other hand, the methods of removal I and others have attempted are not the same as are used in the treatment of malignant disease elsewhere. This consists, as every one is aware, in the free excision of the growth, and of a zone of the surrounding healthy tissue. It would be interesting to know why so many surgeons have not hitherto treated growths in the bladder in the same way as they would treat, for instance, an epithelioma of the lip. Doubtless the frequent presence of a pedicle is to some extent the cause. First, it gives a delusive appearance of innocency; and second, it seems made for the application of clamps and ligatures. However, it has now been proved that the pedicle is not a guide to the nature of the tumour;<sup>2</sup> also that the application of forceps and ligatures cannot remove the growth at its base.

The dread of hæmorrhage has also acted as a deterrent to bold excision. The vascularity of these bladder tumours is well recognised. I have repeatedly seen alarming hæmor-

<sup>1</sup> Butlin ('The Operative Surgery of Malignant Disease,' second edition, 1900, p. 310) states that out of fifty-seven patients who had growths of the bladder removed by partial resection, "the three patients who were alive and free from disease more than three years after the operation had survived respectively three and a quarter, four, and five years."

Those multiple fimbriated papillomata with exceedingly slender stalks are not to be included in this proposition.

rhage follow the use of clamps and ligatures. But, on reflection, it will be perceived that this is exactly what might be expected. Bladder tumours possess capacious blood-channels, with walls which cannot retract or contract. When they are torn the blood is free to pour forth. It is vain to attempt to ligature. On the other hand, the vessels which run through the neighbouring healthy tissues to supply the growth with blood are, although large, few in number, and possess walls capable of retraction and contraction, and are well adapted for the application and retention of ligatures. Lastly, there is the dread of the consequences of incisions which may extend through all the coats of the bladder. But of late years a great deal of evidence has been accumulated, especially from the results of accidental wounds during laparotomies, or accidental rupture of the bladder, to prove that wounds of the bladder unite well and speedily provided that the operation is performed under aseptic conditions. I myself have had very few opportunities of ascertaining the correctness of these inferences, but the following experiences may not be wanting in instruction. In 1897 my colleague, Dr. Griffith, requested me to see a woman aged forty-one years. In December, 1896, she suffered from vaginal pain, especially when she sat down. March, 1897, micturition was frequent, with blood in the urine. In April the bladder pain was severe with incontinence of urine. At the end of April a hard mass could be felt *per vaginam*. It was in front of the neck of the uterus, but not attached to it. *Per urethram* the finger felt a hard mass in the bladder, but its attachments could not be ascertained. The interior of the bladder was very septic. The examination was followed by free hæmorrhage. On April 29th the bladder was abundantly disinfected with biniodide of mercury lotion 1 in 500, and then opened by a free vertical incision above the pubes. The tumour was ulcerated and sloughing. Its widest circumference was afterwards found to be eleven inches.<sup>1</sup> It

<sup>1</sup> "Surgical Registrar's Reports," 'St. Bartholomew's Hospital Reports,' vol. xxxiv, 1898, p. 203.

was attached to the back of the bladder above the opening of the ureters by a pedicle five or six inches in circumference. A semilunar incision was made on either side of the pedicle, and about half an inch from its edge. Several silk sutures were passed through the upper end of the incision and served to bring it together, and to enable the bladder and tumour to be pulled towards the wound. More of these sutures were passed as the tumour was detached. Several large arterial feeders were encountered, but were easily clamped and tied. This had at once a marked effect in lessening the bleeding from the growth. Whilst excising the tumour the vagina was opened, but was closed again with the sutures. Finally, the bladder was again disinfected, and the supra-pubic opening above the pubes closed with a series of silkworm-gut sutures which transfixed the whole abdominal wall, together with the muscular coats of the bladder. A catheter was left in the urethra. During the operation a swelling was felt at the base of the right broad ligament of the uterus. It was thought possible that this was a mass of cancerous glands.

The whole operation lasted an hour and a half, and was followed by a good deal of shock. Although the bladder was washed out twice daily with 1 in 6000 biniodide of mercury lotion the sepsis made headway for a few days, and the supra-pubic wound inflamed and suppurated, and leaked a little urine, but not much.<sup>1</sup>

The posterior wound gave no trouble, and no urine leaked into the vagina. By the beginning of July she was in fair general health and went back home. She died on August 9th, and her death is certified to have been caused by nephritis.<sup>2</sup> This case shows that even when the tumour is very large and vascular the hæmor-

<sup>1</sup> Mercurial lotions have to be used with caution in the bladder as elsewhere. The pain in the bladder is intense if strong solutions are used. In this woman's case the biniodide began to cause some diarrhoea and soreness of the gums.

<sup>2</sup> I am much indebted to Mr. J. F. Jennings, house surgeon, for the trouble he took in obtaining a copy of the certificate of death.

rhage is under control provided (1) that the tumour be not cut into, and (2) that the incision be made in healthy tissues so as to allow of the big feeders being secured. It also helps to show how much the local and general dangers of sepsis can be lessened by powerful disinfectants. I hardly anticipated that the posterior wound would heal so well.

In another instance I excised a stalkless papilloma about three quarters of an inch across, and two smaller ones, which had all been seen with the endoscope. After the excision the raw surfaces were touched with an electrical cautery. The largest of the tumours was too small to be much of a test, but the bleeding from the incision and from the tumour itself was quite trivial. This operation was done in November, 1899. In March, 1902, the woman was quite well, and the urine free from blood and albumen. In November, 1901, she gave birth to a child. The supra-pubic wound was closed with silkworm-gut sutures passed as in the previous case; it healed by first intention, although the urine was faintly alkaline and the growths incrustated with phosphatic deposit. It is recognised that supra-pubic cystotomy is rather easier and repairs better in women than in men, but primary union took place in the case of a man upon whom I operated under almost similar circumstances.

In both the septic condition of the bladder was slight, and probably overcome by the efforts at disinfection. But in addition the endoscopic examination had given a clear and correct idea of the position and size of the growth; thus the proper size of the incision could be judged, a speculum pushed straight over the growth, and no unnecessary bruising or laceration inflicted.

Finally, it is clear that the ideal operation of supra-pubic cystotomy for the removal of tumour from the bladder ought to fulfil the following conditions:

First, an early endoscopic diagnosis.

Second, asepsis before, during, and after the operation.

Third, the excision of the tumour, together with its base and a safety margin of healthy tissue.<sup>1</sup>

Fourth, the closure of the wound left by the excision.

Fifth, the closure of the supra-pubic wound.

I have not endeavoured to discuss many important details; such, for instance, as the best suture material, or the conditions under which drainage is necessary above the pubes rather than by the urethra. In all regions of the body I am accustomed, when sepsis is present, to use biniodide of mercury catgut, and to provide abundant drainage. In addition, it is probable that fine catgut is the best material for all ligatures and sutures, except those in the abdominal wound, and which also close the bladder.

Finally, I am convinced that if the above five conditions were fulfilled supra-pubic cystotomy for the removal of tumours would rapidly take its place in the same rank with the other successful abdominal operations, such as cholecystotomy or ovariectomy.

<sup>1</sup> Obviously this proviso is difficult to fulfil when growth is at the orifice of the ureter, but even there, I believe, we might proceed boldly provided the case is not a septic one. Also, it cannot be fulfilled in cases of general villous papillomata.

## DISCUSSION

Mr. REGINALD HARRISON believed that supra-pubic cystotomy for the removal of large stones or growths was not infrequently fatal by reason of the imperfect drainage thus provided when sacs or pouches were also present. In the child's bladder the latter conditions were uncommon, and the results after this operation were more satisfactory than in the adult. In the adult bladder the addition of independent perineal drainage was often an advantage, as Dr. Fuller, of New York, had shown in connection with his operation for the removal of the entire prostate by the supra-pubic method. Mr. Harrison had never regretted putting in a perineal drainage-tube in these circumstances, but had had instances to regret its omission.

Mr. E. HURRY FENWICK said he had had 500 cases of growth in the bladder with 153 operations, and the death-rate among them was only 11. Hence he thought that an appropriate selection of cases would give a lower mortality than that recorded in the paper. This selection depended on the proper use of the endoscope. No tumour which was so large that it could be felt by the rectum should be touched; as a rule it meant a malignant tumour. The cases referred to in his statistics included quite big operations. The cases which cystoscopy allowed to be attacked and those that it could not were differentiated. A villous single tumour should be removed, but if the tumour were bald it should not be removed. If it were on the upper or posterior wall and single, that portion of the wall might well be removed. If the tumours were kissing they should not be removed, as there would be a connecting tract of malignant tissue between them under the mucous membrane. Pedunculated growths were not always benign, and a case was referred to illustrating this point. It was suggested that rules for operating on tumours of the bladder might be formulated by a special committee of the Society.

Mr. Lockwood, in reply, felt that on theoretical grounds perineal drainage was objectionable as introducing further risk of sepsis, but he had had no practical experience of the method. If cases were taken early enough the risk of sepsis was but trivial. In the case of females *per urethram* drainage was sufficient, and this he thought applied to early cases in males with aseptic urine. The extreme importance of endoscopic the bladder whenever the urine contained blood was insisted on.



A CASE  
OF  
ANEURYSM OF THE ABDOMINAL AORTA  
TREATED BY THE INTRODUCTION  
OF SILVER WIRE

WITH A DESCRIPTION OF INSTRUMENTS INVENTED AND  
CONSTRUCTED BY MR. G. H. COLT TO FACILITATE  
THE INTRODUCTION OF WIRE INTO  
ANEURYSMS

BY  
D'ARCY POWER, M.A., M.B.  
AND  
G. H. COLT, B.A.

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THE patient, a farrier, aged 29, was accustomed to perform heavy work in a stooping position. He had acquired syphilis at the age of seventeen, but had only been treated with mercury for a short time. Three and a half years ago he first noticed something beating in the right side of his abdomen, and since that time he had been continuously under treatment in some hospital or infirmary. On five occasions he received injections of gelatine in the gluteal region, but they had not produced any marked change in the swelling, which increased steadily in size.

On examination he was found to be a sallow, unhealthy, and anæmic man, addicted to morphia. His heart and lungs were reported to be normal. His pulse was regular, but poor in volume, and the radial arteries felt thickened. There was a throbbing area of skin in the epigastric and upper part of the umbilical region, which, at its highest point, seemed to be raised about three quarters of an inch above the level of the surrounding skin. The throbbing was expansile in character, and there was a well-marked bruit, which persisted when the patient was examined in the knee-elbow position. The pulse in the femoral arteries was equal and synchronous. The swelling was diagnosed as an abdominal aneurysm, and more probably an aneurysm of the celiac axis or of one of the branches than of the abdominal aorta.

The sac of the aneurysm was very thin at one or two points, and as the life of the patient seemed to be in danger, it was decided to expose the sac, and either ligature the artery from which the aneurysm arose, or, if this were impracticable, fill the sac with silver wire.

When the operation had been decided upon my attention was drawn to the fact that Mr. G. H. Colt, one of my dressers in the Throat Department at St. Bartholomew's Hospital, had devised and made an instrument for this purpose. When I had seen the instrument I immediately decided to use it in preference to the more usual method.

I cut down upon the most prominent part of the swelling until an exposure of the sac showed that it would be hopeless to ligature the artery, as the sac was densely adherent to the surrounding structures. No coils of intestine lay between the parietal and visceral layers of the peritoneum in front of the aneurysm. I determined, therefore, to wire the sac, and eighty inches of silver wire, with a clotting surface of 3·7 square inches, were rapidly introduced into the aneurysm by means of the new instrument (described later as instrument No. 1). The needle was then withdrawn, the wire was divided, its end was bent up and it was pushed into the sac, the

hole being easily closed with a few Lembert's sutures. The operation lasted thirty minutes from the time the patient was placed upon the operating table until he was removed. The actual introduction of the wire only took two and a half minutes, but even this time might be shortened on a future occasion. The pulse during the operation was 88 and the respirations 20. The operation was performed at 4 p.m., and the patient had a quiet night after a hypodermic injection of morphia at 10.30 p.m. On the following morning (January 21st) his abdomen was soft, his respirations were 18, and his pulse-rate was 136. He complained of abdominal pain over the aneurysm and of pain in his back. A second hypodermic injection of morphia was given at 10 a.m., and the patient then slept quietly for several hours. At 2 p.m. the pulse was 136—144, and at 7 p.m. it was 146. He was ordered two drachms of milk and water every hour, and he was kept under the influence of morphia. There was no evidence of gangrene, nor did he complain of any numbness or tingling in the legs. At 9 a.m. on January 22nd the patient was complaining of pain in his back, his pulse was 160, and his temperature was 101° F. The wound was dressed; it looked healthy. The abdomen was tender, resonant, and showed impaired movement. The right side of the aneurysmal swelling was hard, and did not pulsate, but there was distinct pulsation on the left side. The patient was now taking an ounce of milk and water every hour, and he was reported to have vomited twice, bringing up a small quantity of "coffee-ground" substance the first time, and half an ounce of bile-stained fluid on the second occasion. He still complained of pain in his back, his pulse increased to 170, and he gradually sank, dying at 6.20 p.m. on 22nd January, 1903, about fifty hours after the operation.

The post-mortem examination showed an aneurysm of the size and shape of a large orange projecting forwards from the abdominal aorta between the layers of the transverse mesocolon. The sac was somewhat com-

pressed laterally, and was developed from the aorta itself, the dilated portion of the vessel being about three inches in length, and extending downwards from just below the diaphragm. The great omentum immediately below the greater curvature of the stomach had been torn through at the time of the operation to reach the anterior surface of the sac. On cutting across the aorta just above the diaphragm a loop of silver wire seven inches long was found projecting into the arch of the aorta, but the rest of the wire was irregularly coiled within the sac of the aneurysm. All the other abdominal organs were healthy; the lungs were normal, and the heart was free from disease, except that the pericardium was adherent in places. The aneurysm and aorta were hardened in formalin before a section was made.

There is nothing particularly new in the treatment of aneurysm by the introduction of wire, and I should not have ventured to bring this case before the Fellows of the Society unless I had thought that the apparatus invented by Mr. Colt was sufficiently novel and useful to make it worth while to draw special attention to it. Hitherto the surgeon has been content to puncture the aneurysm with a fine trocar and cannula; he has then withdrawn the trocar and forced the wire through the cannula, from which blood was often flowing with considerable force. The amount of wire introduced in this manner has varied with the time at which the occurrence of kinking arrested its further progress. For this reason it has sometimes only been possible to introduce a few inches when it was intended to have put in several feet. The introduction of wire through a cannula is open to the further objection that a great deal of handling is necessary both by the surgeon and his assistants, so that it is difficult to ensure that the wire last introduced shall be as sterile as that first used.

The factors in the construction of a new instrument were set out as follows:

- (1) The instrument must be self-contained,—that is to

say, it must carry the wire on a reel, and have some form of fine cannula through which the wire is to pass.

(2) It must remove the wire from the reel and force it through the cannula, yet without permitting it to kink.

(3) It must not allow the wire to damage the sac or the surrounding tissues, although some force has to be used in the introduction of the wire ; in other words, the wire must be made to coil up within the sac.

(4) It must be simple in construction, and so easy to work that no instrumental complication may occur during the actual operation, and it must necessarily be capable of withstanding prolonged boiling.

(5) It should, if possible, "snag,"—that is to say, knot or roughen the wire, as coagulation is likely to be promoted by such roughening.

INSTRUMENT I.—After a few preliminary experiments an instrument was constructed to meet these requirements. The instrument works on a principle which may be enun-

FIG. 1.

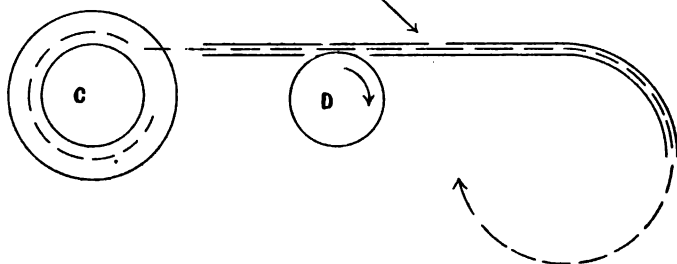


Diagram to illustrate the general principle of Instrument No. 1.

c. Reel.

d. Milling tool which rotates in the direction of its arrow.  
The interrupted line indicates the wire passing from the reel through the needle.

The straight arrow points obliquely to the opening for the stilette.

ciated in the following terms. If what is known to the mechanical engineer as a milling tool be made to revolve at a distance less than the diameter of the wire employed from the inner surface of the dorsal wall of a hollow

needle, the ventral wall of which has been cut away, the milling tool will grip the wire between itself and the needle, and will wind it off a reel and drive it through the needle with a force only limited by the force at the disposal of the operator. It will at the same time "snag" or mill the wire (Instrument I, Fig. 1). To carry out this principle a quarter-curved tubular needle was embedded for about two inches of its length in the substance of a brass carrier. A semicircular incision was then made down to it through the brass, so that the lumen of the needle was exposed. A milling tool was introduced at this spot to compress the wire with a steady grip as it passed through the needle, the pressure being made between the milling tool and the dorsal wall of the needle, and care was taken that no space should exist in which the wire could kink. The mounting of the needle was then bolted to the mounting which carried the milling tool, which was so geared up as to give the operator room to use the instrument without getting his hands too near the wound. A second hole was made into the tubular needle distal to the milling tool, and along this a stilette is passed to block the point of the needle whilst it is being pushed into the sac of the aneurysm. The instrument is further provided with a handle by which to hold it, and with a second handle which, when turned, causes the milling tool to revolve.

The method of use is as follows:—The aneurysm is punctured on the right-hand side, the stilette is withdrawn, and blood flowing through the needle shows that the point is lying in the sac. The handle to which the milling tool is geared up is then turned in the direction of the arrow engraved upon it, and the wire is wound steadily and rapidly through the quarter-curved needle. The wire emerges into the aneurysm in a coil measuring one and five eighths inches in diameter, the coil increasing spirally from right to left so as to produce a loosely formed spring. The wire is milled as it passes under the milling tool on the axial surface of the spiral,

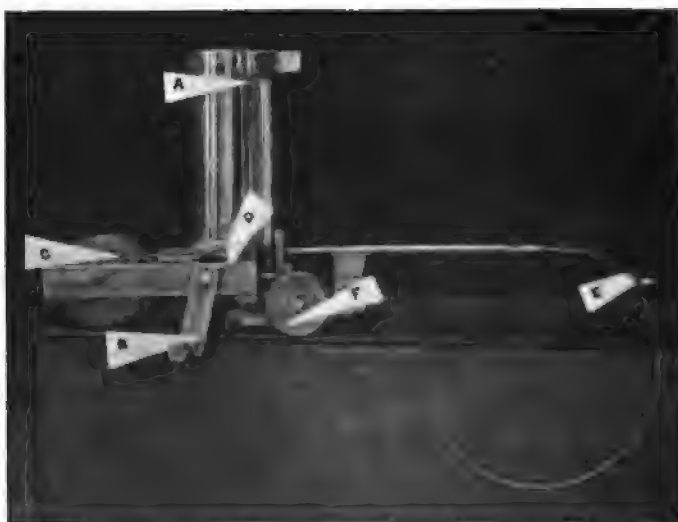
the coils of which are parallel and one eighth of an inch apart. This arrangement of the coils is ensured by slightly curving the needle in a plane at right angles to its axis and to the plane of the quarter-curve. Five turns of the handle introduce two complete coils of the wire, the length of which is approximately ten inches, and the clotting surface at least 0.46 square inch. It is evident, therefore, that, although the point of the needle is out of sight, a fairly correct estimate can be made of what is happening within the sac of the aneurysm. When a sufficient quantity of wire has been introduced the needle is withdrawn, the wire is cut, is looped upon itself—to prevent the sharp end from injuring the sac,—and is pushed into the aneurysm. The hole in the sac is afterwards closed by a few point sutures.

The use of this instrument in the case narrated at the beginning of the paper shows that although it worked smoothly it did not quite fulfil all the requirements of the case, for it allowed a loop of the wire to travel out of the sac and seven inches up the aorta. An examination of the specimen shows that this diverticulum of wire was not carried into the aorta by the blood-stream, because it has gone upwards or against the direction of the blood-flow. The majority of the coils, too, are firmly implanted in blood-clot in the sac of the aneurysm. The real explanation seems to be that whilst the wire was being introduced into the sac some of the coils became hampered in their revolution, and the wire was driven out in a loop at one point. A further hampering then occurred, and the coils of wire no longer revolved, until the resistance to the further introduction of wire became so great that it could not be overcome by the milling tool, which then slipped upon the wire instead of biting it.

The best method of preventing such an accident on another occasion would be to introduce the wire so that the coils are not all in one piece. This can be done by dividing the wire into sets of coils, a method which has

the further advantage of diminishing the ever-increasing resistance to its introduction. It does not seem possible to make one length of wire push the previous length through the needle into the sac, partly because the wire is too fine, partly because it does not exactly fill the needle when it has been milled, and partly because it is inconvenient to feed a needle with detached lengths of wire. As a matter of experiment, when such an attempt is made the two sections either jam in the needle or the hinder piece of wire kinks. The only alternative

FIG. 2.



Flag labelled side view of instrument No. 2, about one third natural size. Enlarged from a photograph taken by Dr. E. H. Hunt.

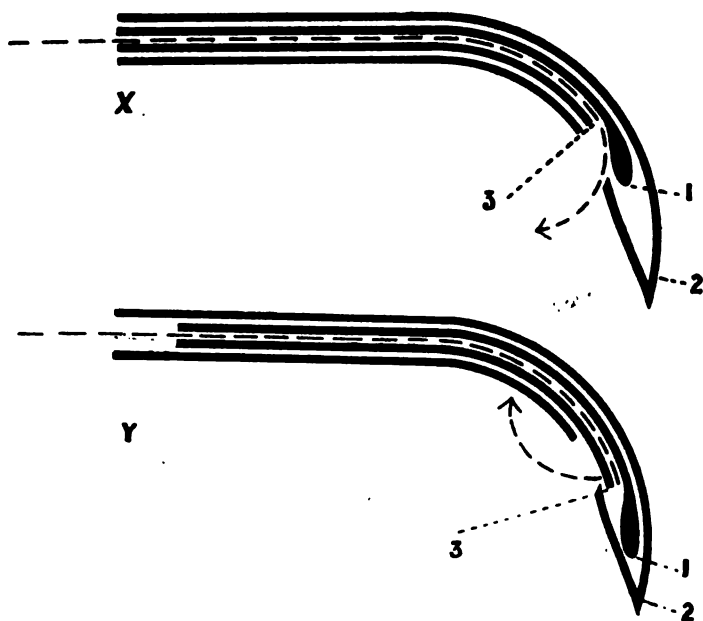
- A. Fixed handle for operator's left hand.
- B. Moveable handle for operator's right hand.
- C. Reel.
- D. The arch is the situation of the milling tool.
- E. Placed between the lateral eye of the outer needle and the coil of wire emitted. Near  $\pi$  the dorsal opening into the inner needle is seen.
- F. Stud by means of which the outer needle is caused to slide over the inner needle. A portion of the rackwork with its stop is seen between F and B.



therefore, seems to be to cut the coils as they leave the eye of the needle, and this must be done without withdrawing the needle from the sac of the aneurysm. The wire can be divided in several ways, but the method now to be described seems to be the simplest and most practical.

INSTRUMENT II.—The second instrument (Fig. 2) differs in many important points from the first instrument.

FIG. 3.



Diagrams to show how the wire is severed at the lateral eye of the needle.

1. Inclined plane at the end of the inner needle.
2. Outer needle.
3. Cutting edge of inner needle.

In Fig. X the wire, represented by an interrupted line, after impinging on the inclined plane emerges as shown by the arrow.

In Fig. Y the outer needle has been retracted over the inner, and has severed the wire at 3.

There are no gear-wheels, and the milling tool is driven direct. The needle is sufficiently long to remove the

mechanism to a distance from the wound. Lastly, the instrument is able to take a thinner wire, and a stilette is not required. The coils are divided by the following mechanism (Fig. 3) :—The hollow needle (Fig. 3, x) along which the wire travels is encased in a second needle (Fig. 3, x, 2), which exactly fits it. The end of the inner needle is completely blocked up by a minute inclined plane made of steel (Fig. 3, x, 1, and y, 1), which is securely brazed in position, and is so arranged that it faces the oncoming wire. A lateral opening is made through both needles at their distal ends, and in such a manner that an eye is made with the depressed edges seen in the better kinds of Jacques' rubber catheters. When the two hollow needles are accurately adjusted (Fig. 3, x) the lateral opening is continuous from the inside of the inner needle to the outside of the outer needle, and through this opening the wire is directed by its impact on the inclined plane (Fig. 3, x, 1) which blocks the end of the inner needle. The tube of the inner needle is soft and flexible, except at the eye, where it is tempered. The outer needle is quarter-curved, tempered throughout, and pointed (Fig. 3, y, 2). The inner needle adapts itself to the curve of the outer needle in all relative changes of position. The outer needle is attached to a rack and pinion placed close to the hand of the operator, and a movement of the pinion causes the outer needle to slide over the inner needle (Fig. 3, y). The relation of the lateral eye of the outer tube to the lateral eye of the inner tube is thus altered, and by the position of a stop on the rackwork the operator knows the relative position of the two eyes, even when they are hidden from his view. The alteration in the two parts of the eye is sufficient to divide the wire, which may thus be guillotined wherever and as often as the operator chooses. The pinion is reversed when the wire has been divided until the stop is encountered, when a fresh series of coils can be introduced into the sac of the aneurysm.

The wire employed is No. 27 on the standard wire

gauge, and is 0.0164 inch in diameter, or rather less than half a millimetre across. It is soft annealed silver wire, and is supplied by any large firm of wire-drawers at six shillings an ounce of about twenty-two yards. It is flattened by passing under the milling tool, and it is then 0.0215 inch in width and 0.0142 inch in thickness; and it has a slightly increased surface area, the surface area of the original wire being 5.152 square inches per length of 100 inches. It is exquisitely flexible after it has passed under the milling tool, and easily bends in the plane of the coil, though it is relatively rigid to stresses in any other plane. It is hardly possible to imagine it causing

FIG. 4.

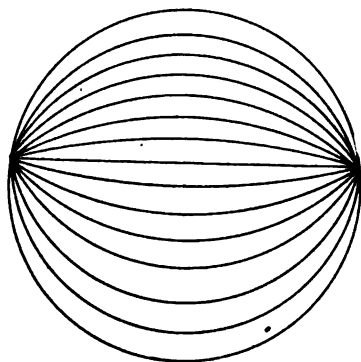


Diagram of ideal arrangement of expanding cage.

any damage inside an aneurysmal sac, and it is in the highest degree unlikely that it would pierce the wall. The diameter of a coil is three and a quarter inches, but a coil readily adapts itself to the wall of a cavity smaller than itself.

With this instrument ten turns of the handle introduce two complete coils of wire or a length of twenty inches. When the instrument is used to wire a large aneurysm five turns of the handle should be made before the wire is guillotined, for if fewer turns are made less than a coil is introduced, and when small pieces of wire are allowed

to sink in the sac of an aneurysm there is a danger that they may be carried out into the general blood-stream with unsatisfactory results.

**INSTRUMENT III.**—Another method of wiring aneurysms consists in the introduction of one or more cages of steel wire. The cages can be compressed into a cylinder which can be easily passed through a fine cannula into the sac of an aneurysm, when they immediately expand in the manner shown in Fig. 5.

The model when compressed is five inches in length and one sixteenth of an inch in diameter. It consists

FIG. 5.

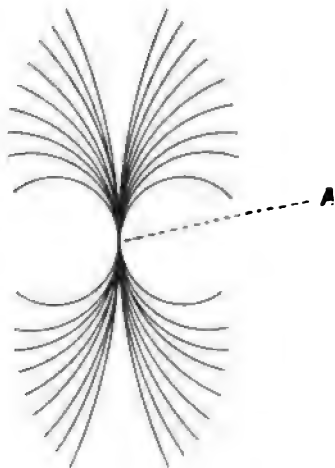


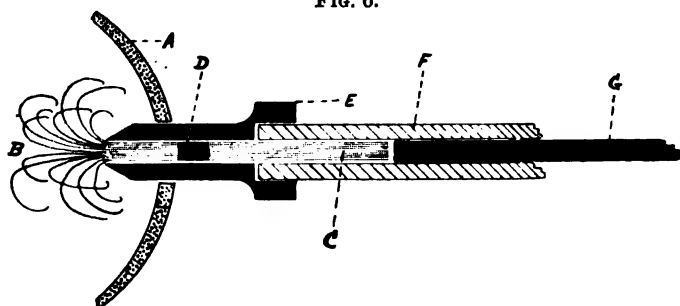
Diagram of actual arrangement of expanding cage. It can be compressed to its diameter at the central part (A), and after traversing a fine cannula will expand again.

of thirty wires, each measuring 0.008 inch in diameter and five inches in length. The cage when it is expanded fits a sphere three inches in diameter, but it can be made of any size. The total surface area of each cage is as nearly as possible two and a half square inches, which is almost equivalent to fifty inches of the silver wire used in Instrument II.

The cage is compressed when it is to be used, and is inserted into a cylindrical tube or cartridge which exactly fits a collar on the cannula employed to traverse the sac of the aneurysm. The cage is expelled from the cartridge through the cannula into the aneurysmal sac by pushing it home with a wire ramrod. More than one cage can be introduced if it is thought desirable to increase the clotting surface, but when a process of active clotting is once started in an aneurysm it is usually progressive, and there is some danger that the second cage may push the first one into an undesirable position.

An ideal wire cage of a spherical shape is shown in Fig. 4, but it is difficult to make and unsatisfactory in action. Fig. 5 is a diagram of the actual arrangement adopted, and Fig. 6 shows it in operation, but an objection

FIG. 6.

Diagrammatic section through Instrument III *in situ*.

- A. Sac of the aneurysm.
- B. The cage expanding.
- C. The cage compressed.
- D. Solder at the centre of the cage.
- E. Collar on the cannula.
- F. Cartridge.
- G. Ramrod.

If c be considered absent, D to B would represent a "wisp" entering the sac.

to it is that the second half of the cage does not expand until it is completely freed,—that is to say, until the first half has moved onwards about two and a half inches from the end of the cannula. This might lead to forcible

damage to the opposite wall of the sac by the half already introduced. It can be prevented by using only a half cage or "wisp," which, having completely expanded after traversing the cannula, is at once set free in the sac.

Experience may suggest different forms of wire cage, but for the present the wiring of aneurysms by means of a wisp appears to be the more satisfactory method. The chief reasons for this are that the apparatus required is exceedingly simple, and that this part of the operation can be accomplished in a very short time. In a suitable case it could be performed under cocaine, or without any anæsthetic, as in tapping a hydrocele. Thus in five seconds from the time of puncturing the sac a sterile foreign body presenting a clotting surface of relatively large value can be placed in position in the aneurysm with very slight risk of its injuring this structure, or of its moving about when once it is in position. Care is taken to make the puncture in a direction estimated, as far as possible, to be parallel to the plane of communication between the sac and the vessel from which it arises, and to arrange for closing the puncture wound before withdrawing the cannula. Thus it is clear that from the time the cartridge replaces the trocar of the cannula the method of procedure will be nearly a bloodless one, and not likely to frighten a patient only under the influence of a local anæsthetic; and what has been found to be one of the chief objections to performing the operation without an anæsthetic is to a great extent removed, and the procedure as a whole greatly facilitated.

# THE TREATMENT OF ANEURYSM BY SUBCUTANEOUS INJECTION OF GELATINE

BY

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ANEURYSM is such a desperate disease, and one which so frequently terminates in a tragic and sudden manner, that any treatment which offers a fair chance of success deserves to be seriously considered.

The method of subcutaneous injection of gelatine, first recommended by Lancereaux in 1897, is the latest and most promising medicinal means by which it has been attempted to lessen the dangers and miseries attendant upon aneurysmal dilatation of an artery.

A fuller knowledge of Lancereaux's means of cure and of its capabilities for good or evil can only be achieved by a record of the results attained in the cases subjected to the treatment which he advocates. That the risks are

considerable is amply evidenced by the recent unfortunate experience at Guy's Hospital, where two patients died from tetanus in the course of treatment by this method. Both patients—the one a carter aged 37, and the other an engineer's labourer aged 33—were the subjects of aortic aneurysm; but though these men died from tetanus, a third patient, who was, about the same time, treated in the same way for the same disease, was discharged from the hospital apparently cured. Too much stress must therefore not be laid upon the unfortunate result in the cases referred to, and it must not be concluded that the tetanus spores, highly resistant though they are well known to be, existed in the gelatine used, which had been carefully subjected to prolonged and thorough processes of sterilisation. The fact of the third patient having escaped such an untoward complication is, indeed, of itself almost sufficient evidence that the contamination arose not from the gelatine, but from some outside source which it was found impossible to trace. Though Lancereaux's plan of treatment seems to have failed in some cases, there are many in which it has been attended by results sufficiently brilliant to attract attention and to warrant hopeful anticipation. Where an aneurysm is so situated that it can be dealt with by surgical methods, these will probably continue to be regarded as the safest and most reliable means of treatment to which the patient can be subjected; but in cases—and they form no small proportion of the sum total of this formidable disease—which are beyond the reach of the surgeon's aid, any means by which the misery and suffering may be mitigated, or the risk of sudden death from rupture lessened, must be welcomed as an advance in the progress of the therapeutic art.

In a paper communicated by Lancereaux and Paulesco to the '*Bulletin de l'Académie de Médecine*' in July of 1901, it was pointed out that non-success often arises either from faulty application of the method, or from its use in cases of fusiform aneurysm, where the chances of amelioration are comparatively slight. In 1895 M. Dastre



claimed to have proved that the injection of a solution of gelatine into the veins of a dog rendered the blood more coagulable; but his results are not universally accepted, and it seems not yet to be certain how far the injection of gelatine into the cellular tissue of human beings can produce an effect on blood-coagulability. Nevertheless there is a considerable mass of evidence which goes to prove that it undoubtedly does exert such an influence. It is difficult otherwise to explain the marked improvement as regards their most urgent and painful symptoms which aneurysmal cases experience when treated by it. If a restricted diet and complete rest in bed are associated with the use of gelatine, improvement from these measures may readily be fallaciously ascribed to the injections; but cases do occur in which patients have failed to respond favourably to the ordinary and accepted dietetic, drug, and rest treatment, and yet have experienced striking relief when to these influences have been added that of gelatine injected into the intermuscular spaces.

The first use of gelatine as a curative injection for aneurysm was reported by Lancereaux to the French Academy of Medicine in June, 1897. The patient was an embroiderer aged 46 years, who presented all the classical signs and symptoms of an aneurysm of the ascending aorta, which had advanced to such a stage that the skin over the surface of the tumour was thin and ecchymotic. On January 20th a first injection of 20 c.c. of a sterilised saline solution of gelatine was administered into the subcutaneous tissue of the left buttock. Following on this, Lancereaux's report tells us, there was produced a little redness at the seat of injection, and the temperature rose to 38°C. The next day a normal condition was re-established, and in addition it was demonstrable that the tumour had become manifestly more firm and the pulsations less forcible. For some days afterwards it diminished a little in volume, and—what was still more remarkable—the pain completely disappeared and the patient was able to assume the dorsal position without experiencing either oppression

or paroxysmal cough. But soon the tumour resumed its original dimensions; its walls again became soft, and the blood could once more be felt forcibly driven against the skin, while coincidentally the intercostal pains reappeared. A fresh injection of 150 c.c., made on February 10th, was followed by the same result as the first, but this time without reaction either local or general. Subsequently eleven similar injections were given at intervals of a few days, the last being administered on May 7th. By that time the tumour had diminished by two centimetres in the vertical and one centimetre in the transverse diameter; it was very firm, and on palpation, though pulsations could be felt, they were pulsations *en masse* transmitted by the aorta, and not expansile pulsations such as the patient presented when first seen.

The man no longer suffered any pain, and so strongly insisted on going out that he was discharged on May 25th. "In face of this result," says Lancereaux, "which was achieved under our observation, it is difficult, if not impossible, despite therapeutic scepticism, which is not inconsistent with an ardent faith in medicine, to refuse to the means employed a substantial utility, for without it our patient would have perished. Therefore we do not hesitate to recommend this method of treatment with which we have succeeded, more particularly since it is harmless, and the only one applicable for the treatment of such internal aneurysms as are beyond the reach of surgical interference."

At a subsequent meeting of the French Academy on October 11th, 1898, Lancereaux presented another report on this new treatment, and recorded in detail five cases, in three of which complete cure had resulted, while in the remaining two death had occurred, in one instance from rupture of the sac, and in the other from uræmia. He thus sums up the conclusions which were to be drawn from this further experience:—"Gelatine introduced into the subcutaneous cellular tissue penetrates into the blood, which it renders more than normally coagulable; and

since this blood encounters in the aneurysmal pouch two conditions favourable to coagulation—namely, a retardation of its current, and a vascular wall which is frequently uneven,—there is produced a more or less abundant formation of clots, which in time fill up the sac. Ultimately these clots contract, the pouch which contains them diminishes in size, and the pressure symptoms to which it gave rise diminish and disappear. If softening of the clot takes place the blood penetrates between it and the walls of the sac, and the tumour is reproduced. Under such conditions, fortunately, coagulation again takes place readily. Gelatine, therefore, constitutes an excellent therapeutic agent, which, if it does not cure true aneurysms, at least favours the natural process of their cure.”

At a meeting of the Académie de Médecine held on July 16th, 1901, Lancereaux and Paulesco related four further cases, all considerably improved, if not permanently cured. Good results have also been recorded by, among others, Geraldini (*Gazz. degli Osped.*, February, 1900), Buchholz (*Norsk. Mag. f. Laegevidensk.*, February, 1900), Barth (*Münch. med. Woch.*, April, 1901), Sorgo (*Zeits. f. klin. Med.*), and Mancini (*Rif. Med.*, May, 1902).

At home the treatment does not seem, so far, to have been received with much enthusiasm, nor practised with much perseverance; but stray cases are recorded here and there throughout our medical literature of the past two years, and I understand that Dr. Maguire, of the Brompton Hospital, is about to publish the results of his experience in a short series of patients treated by the gelatine method.

The following four cases go some way towards confirming the favourable view which Lancereaux has advocated. By experiment Lancereaux fixed the quantity of gelatine necessary to obtain a sufficient coagulability of human blood at 250 c.c. of a saline solution containing two grammes per 100 c.c. of gelatine, and from experience he found that several months are required during which at

least from twelve to fifteen injections are necessary to achieve satisfactory results.

According to Huchard, a 1 per cent. is safer than a 2 per cent. solution of gelatine, and an interval of from eight to ten days is advisable between each injection. I have not found it possible to introduce into the subcutaneous tissue more than 100 c.c. without producing local pain, and I have observed that even this amount must be injected slowly—over an interval of ten or twelve minutes—in order to avoid discomfort and over-distension of the skin. A considerable swelling is produced at the seat of injection, but this entirely subsides within from six to twelve hours. The inner aspect of the thigh has been found a more convenient situation than the buttock; in one case where the pectoral region was chosen the patient complained of so much pain that the experiment was not repeated. In all these four cases the patient was kept during his course of treatment confined to bed, and the injections were repeated twice a week.

Concurrently with the gelatine treatment, iodide of potassium was given in ten-grain doses three times a day, and with it was combined minim doses of a 1 per cent. solution of nitro-glycerine whenever the pulse tension became excessive, or when there were anginal symptoms.

The nitrogenous elements of the daily dietary were minimised, and the amount of liquid allowed was kept within narrow limits.

The apparatus used by Lancereaux is somewhat complex; it will be found fully described at page 358 of the fortieth volume of the 'Bulletin de l'Académie de Médecine.' At Greenwich we contented ourselves with a glass syringe of 100 c.c. capacity, having metal fittings and an adjustable piston.

The gelatine solution was made after the following method, for the description of which I am indebted to Mr. Hart, who was responsible for its preparation:—  
"Gelatine, 1 ounce; chloride of sodium, 131 grains; sterile distilled water to 50 ounces. These are put into a flask,

plugged with cotton wool, allowed to stand an hour or two for the gelatine to soften, and then the heat from a water-bath applied to effect solution. The flask is afterwards placed in a steamer for an hour, and is subjected to this treatment on three consecutive days. Immediately before use the quantity to be employed—100 c.c.—is again re-steamed." Every precaution was taken to ensure complete asepsis, not only of the solution, but also of the patient's skin and of the instruments used.

The following account of the cases has been kindly compiled for me from the hospital records by Dr. Oswald Marriott.

*Aneurysm of the Arch of the Aorta.*

John McC—, fireman, aged 35, admitted on April 1st, 1902, for pain in the chest, with a pulsating tumour in the median line about the level of the second and third costal cartilages.

The patient had noticed the pain for about five months. It first interfered with his doing his work at St. Helena in November, 1901, on the outward voyage to the Cape. On arrival at Port Elizabeth he had to go into hospital on account of constant pain and dyspnœa. Since then he had not been fit for any work, and latterly had been unable to sleep at nights except for short snatches, and then only if propped up in bed. The pain radiated down both arms, but was most severe on the right side. There was a definite history of syphilis contracted fourteen years ago. He was addicted to alcohol, and admitted that during the few weeks he had been ashore he had been drinking very heavily.

*Condition on admission.*—The patient was a well-built and well-nourished man. He complained of constant, dull, heavy pain and distress in his chest, more marked on exertion. He was breathless, and quite unable to lie down in bed on account of dyspnœa. The pulse was regular and of medium tension. The right radial was stronger than the

left radial pulse. Temperature  $98.8^{\circ}$ ; respirations 24 per minute.

On inspection, in the middle line of the chest, about the junction of the manubrium with the body of the sternum, there was a large, circular, pulsating swelling causing protrusion of the bony and cartilaginous chest wall. The superficial diameter of the pulsating area measured 5 inches transversely and  $3\frac{1}{4}$  inches vertically. The skin over the swelling was red, tense, and painful. The pulsation was synchronous with the heart-beats, and on palpation was markedly expansile. The note on percussion over the swelling was dull, and the act of percussion caused a considerable amount of pain. The cardiac impulse was seen in the fifth left intercostal space in the nipple line; it was diffused and heaving; no thrill was detected. Over the cardiac impulse the first sound was impure, but on auscultation upwards towards the tumour the muffled sound acquired the character of a murmur. Over the tumour itself was heard a distinct systolic bruit, followed by a loud accentuated second sound. There was fulness and throbbing in the vessels of the neck. Tracheal tugging was well marked. There was no notable impairment of the percussion note over the lungs, but on the right side, behind, the air-entry was diminished, and the respiratory murmur was high-pitched and almost bronchial in quality. Voice-sounds were normal. The total area of hepatic dullness measured vertically in the nipple line  $4\frac{3}{4}$  inches. There was a space of two inches between the upper margin of hepatic dullness and the lower margin of the pulsating tumour, over which the percussion note was clear. The pupils were large and equal; they reacted to light and accommodation. No alteration or impairment of movement of the vocal cords was noticed. Both patellar and plantar reflexes were normal.

*Progress and treatment.*—After a week's rest in bed, during which the temperature varied between  $97.6^{\circ}$  and  $99^{\circ}$ , and the patient was always supported in the sitting position with a bed-rest, gelatine injections were advised.

His distress was so great that he readily acquiesced. He was kept on a light nutritious diet, the liquid constituents being strictly limited. Alcohol was entirely withheld. He was also ordered a mixture containing iodide of potassium, carbonate of ammonium, and cinchona.

The front and inner surfaces of the thighs were shaved, and the skin cleansed with antiseptics. The first injection contained only 15 grains of gelatine in about 50 c.c. of saline solution, the solution having been sterilised on three separate occasions and raised to boiling-point just before using. All instruments—the needle (a large exploring needle), the syringe (a glass syringe of 100 c.c. capacity), and the glass bottle—were also carefully sterilised by boiling. The puncture was made through the skin of the inner aspect of the thigh, about two to three inches above the patella, and the solution was injected warm. After withdrawal of the needle a gauze and collodion dressing was applied, also a pad of antiseptic wool with bandage to prevent irritation of the skin by contact with the clothes. The local swelling round the seat of puncture disappeared in about six hours. Every subsequent injection contained 30 grains of gelatine dissolved in 100 c.c. of sterilised saline solution. The injections, to the number of twenty, were given twice a week into each leg alternately. The temperature frequently rose to  $99^{\circ}$  on the night of the injection, and on three occasions just exceeded  $100^{\circ}$ , but otherwise no abnormal symptoms ensued. Complete rest in bed throughout the treatment was insisted upon.

The pain gradually disappeared; the patient slept well at night, and was, after a short time, able to lie down flat. He expressed himself as getting daily better, and was always anxious to be up and about. After he was allowed to leave his bed his movements and exercise were gradually increased, and he asked for his discharge from the hospital on July 9th, 1902, saying he felt no trouble in his chest at all. The pulsation was very much diminished; there was no pain on palpation, nor on slight pressure over the tumour.

The patient was seen ten days after his discharge. He admitted that he had been drinking heavily while out of hospital, and had been detained in one of the London infirmaries two nights previously on account of alcoholic coma. He had some return of pain, but the signs were unaltered, and with a few days' rest in bed his pulse quieted down and the pain disappeared again. He had had no trouble at the site of injection on the thighs.

*Abdominal Aneurysm.*

William W—, fireman, aged 47, admitted on April 26th, 1902, for severe pain in the epigastrium. The epigastric pain had been so acute as to interfere with his doing his work for the last five weeks; previously there was pain, but much less severe. Lately it had been more or less continuous, and was generally worse after food. It was of a tearing character, and prevented the patient from lying down or keeping still. It radiated through to his back. Sometimes there were exacerbations of acute pain, which quite "doubled him up."

The patient was a West Indian. He readily owned to having freely indulged in alcohol when ashore, especially in spirits. The history of syphilis was indefinite, and there were no corroborative signs. He was married and had several children.

*Condition on admission.*—Patient was a tall, well-developed man. Temperature 98°. Pulse 70, regular, full, and soft. The femoral pulses were equal, and synchronous with the radial pulses. Respirations 20 per minute and regular. The cardiac impulse was visible in the fifth intercostal space, half an inch internal to the nipple line. The precordial area of dulness was not increased. The heart-sounds at the apex and over the second right and left spaces were normal. The abdominal walls were lax and thin. On careful inspection just below the epigastric notch, and rather to the left of the median line, there was a circular area of pulsation, which corresponded with an ill-defined, readily felt tumour. The pulsations were ex-



pansile and synchronous with the heart-beats. There was marked tenderness on palpation over the epigastrium. The liver was just felt below the costal margin. Spleen not palpable. On percussion over the tumour the note was dull. The dulness was not continuous with the hepatic or splenic areas of dulness. Pain was complained of on even slight percussion. On auscultation over the centre of the tumour a loud systolic bruit was audible; this was quite localised, and lost immediately below the tumour. No abnormal or adventitious signs were present in the lungs. Though the patient occasionally experienced pain shooting round to the back, there was no tenderness on pressure over the vertebral spines behind, or on pressure of the occiput downwards. The urine had a specific gravity of 1014, was neutral in reaction, and contained no albumen. The patellar reflexes were present and normal.

*Progress and treatment.*—The patient was kept at rest in bed, with light, nutritious diet and limited liquids, for three weeks. He was unable to lie down for many days, and hypodermic injections of morphia were necessary for the first fortnight to ensure rest at night. He also had 15 minims of Liquor Morphiæ Hydrochloratis six-hourly by the mouth. The bowels were kept acting freely. The condition was explained to the patient, and he decided to undergo the treatment by subcutaneous injections of gelatine. The first injection was given on the twenty-first day after admission. The inner aspects of the thighs were shaved and made thoroughly aseptic, and they were injected alternately—each thigh being used once a week. Twelve injections were given. The first contained 15 grains of gelatine in 50 c.c. of sterilised saline solution, and every subsequent injection contained 30 grains in 100 cubic centimetres. There was no disturbance of temperature except on two occasions, on each of which it rose rapidly to 103°, but fell within twenty-four hours. On both these occasions the injections had been given under the skin covering the pectoral muscles.

The pain disappeared absolutely, and the patient was allowed up and ordered gentle exercise. He asked to be discharged eighteen days after the injections had been stopped. During the week before his discharge he was frequently given leave to visit the docks, in order to arrange to get a berth home. This exertion caused no recurrence of pain. On examination before leaving hospital a small, oval, firm mass, about the size of a hen's egg, could be felt between the fingers and thumb; it was quite circumscribed and localised to the left side of the median line, and about two inches below the ensiform cartilage. There was no pain on palpation. The systolic bruit persisted, but remained localised. He was seen one month later, before he left for the West Indies. The improvement was then fully maintained, and he expressed himself as grateful for being so completely relieved of his symptoms.

*Aneurysm of the Ascending Aorta.*

William S—, seaman, aged 50, admitted on May 1st, 1900, for pain in the chest. There was no history of alcohol or rheumatic fever, and no record of syphilis could be obtained. Patient was a West Indian by birth, and had been a seaman all his life.

*Condition on admission.*—On examination the cardiac impulse was seen in the fifth space on the left side, and was situated half an inch internal to the nipple line. There was visible expansile pulsation in the second right intercostal space, and less marked pulsation in the first space. On percussion the precordial dulness was increased transversely, and the note was dull over the area of pulsation, which extended from the first to the third rib on the right side and outwards to two inches to the right of the manubrium. On auscultation at the apex the sounds were normal; in the second left space the second sound was accentuated. Over the second right space was heard a loud systolic murmur two fingers' breadth from

the right edge of the sternum, and also a diastolic bruit conducted down the sternum. The radial pulses were unequal, the right being the stronger and the left slightly delayed. The carotid pulses were alike. The pupils were normal. No alteration of movement of the vocal cords was detected. No abnormal physical signs were found in the lungs or abdomen, but there was some expectoration, which was occasionally blood-stained. The urine was clear, neutral in reaction, and with a specific gravity of 1010; it contained no albumen.

*Progress and treatment.*—The patient was put on a light diet, the amount of fluids being limited. He was kept at rest in bed, and a mixture containing iodide of potassium and cinchona was ordered. On the eighteenth day after admission the subcutaneous injection of gelatine was started, and a solution containing just over 20 grains of gelatine was injected under the skin on the inner side of the thigh, the skin having been previously shaved and cleansed in the usual way. The injections were continued twice weekly after this, and the full amount of 30 grains in 100 c.c. of sterilised saline solution was given each time. There was slight reaction on several occasions at first, the temperature rising within twelve hours to 100° or 101°; and on one occasion some temporary local inflammation ensued at the seat of injection. The injections were given in the thighs alternately. The last, which was the twentieth, was administered on January 27th, 1901. There was then no visible pulsation in the chest, but the throbbing tumour was replaced by a firm resistant mass, which on palpation still pulsated, but faintly and without expansile extension. The impulse was still half an inch internal to the nipple line. There was a to-and-fro murmur in the aortic area, and a systolic and short diastolic bruit at the apex. The patient was allowed out of bed, and his exercise was regulated and gradually increased. He had no recurrence of pain, and left the hospital on March 13th, 1901. For the week previous to his discharge he walked round Greenwich Park and Blackheath for two or three hours

every morning without discomfort. Patient was seen three months later, and then expressed himself as still feeling quite well. Subsequently he returned to the West Indies.

*Aneurysm of the Ascending Aorta.*

William W—, seaman, aged 57. This man first came under observation in March, 1899. He improved during four months' treatment in hospital, and remained out for three months; he was then in the hospital again for five months, during which he was treated with gelatine injections.

*Condition on admission.*—The patient was a vigorous man, but had lost weight recently, and only scaled 11 st. in 1899. He had been a seaman all his life. No absolutely reliable history of syphilis was obtainable. No history of rheumatism. He first noticed pain in his chest in February, 1899. On examination there was some flattening of the upper part of the thorax, especially on the right side. The cardiac impulse was seen in the fifth left intercostal space in the nipple line. Pulsation was visible over the whole sternum and over the third and fourth intercostal spaces on the right side. The precordial dulness extended from the left nipple line to the right sternal margin below the level of the third rib; above this level the percussion note was dull behind the sternum up to the level of the first costal cartilage. No thrill was felt, but in the fourth left space a sudden movement was detected accompanying the second sound. On auscultation at the apex the first sound was not well defined. In the second right space an occasional systolic murmur was heard. The radial pulses were unequal, the left being stronger than the right. The pupils were unequal, the left being larger than the right. There was slight œdema over the lower part of the chest on the right side, but this cleared up after seven days. "Tracheal tugging" was indefinite. Over the upper part of the chest on the right

side the breath-sounds were feeble, and behind a few mucous râles were heard at the apex and base. There were no signs of pressure on the trachea or œsophagus. Slight prominence of the upper dorsal vertebræ and corresponding ribs on the right side behind was evident.

*Progress and treatment.*—The patient required frequent hypodermic doses of morphia to produce sleep.

Gelatine injections were commenced on October 12th, 1900, and were given twice each week. The pain quickly subsided, and after fifteen injections the patient was able to get up, having been in bed for many months. His convalescence was slow, but after a few weeks he could walk about comfortably, and went home on being discharged from hospital. He afterwards presented himself once a month for examination, and could always get about well without dyspnœa or recurrence of pain.

The experience derived from such a small number of cases is not enough from which to formulate definite conclusions, but, so far as it goes, it tends to show—

1. That gelatine injections may, with proper precautions, be given subcutaneously with safety.

2. That they produce a marked and speedy decrease in all the subjective, and in some of the objective symptoms presented by internal aneurysms.

3. That this relief of symptoms is only explainable on the theory of a diminution in pressure-effects from shrinkage in size of the aneurysmal sac.

4. That this diminution in size, accompanied with marked increase in the resistancy of the tumour wall, was capable of physical demonstration in three of the cases treated.

5. That the after histories of the patients, so far as they could be obtained, afforded evidence that probably the beneficial results were permanent; and that, at least, they had not been seriously invalidated by the habits and exertions of the patients between the date of their discharge and that of their being last seen.

## DISCUSSION

Dr. R. MAGUIRE had treated eight cases of aneurysm by the gelatine method; in seven there was considerable improvement, and in the other there was but little to effect, as the aneurysm was almost cured beforehand. Details of three of the more instructive cases were given. In one case an aortic regurgitant murmur was noticed to disappear under treatment: it became inaudible after the third injection, suggesting that it was caused by the stretching of the aorta and not by disease of the valve; moreover the sac was seen to contract under daily injections. In another case the patient returned to his work as a carpenter, but eventually died from "weakness." In a third case there was a large bulging mass to the left of the sternum, and the skin seemed to be about to give way, when the patient was treated for six weeks with three sets of four consecutive daily injections, an interval of two weeks between each set, with the result that he was now doing his work and feeling perfectly well. Examination with the X rays in this case now showed no visible expansion of the aneurysm. The ordinary medical treatment of aneurysm of the aorta was disappointing; it was also the cause of much distress to the patient. But there was some danger in the gelatine injections. His first patient died from tetanus, as he believed, and similar cases were recorded at Guy's Hospital. In this case the patient's house was in a garden, the room itself contained plants, and it was suggested that the germs came from the outside. A mechanism to prevent the contamination of the gelatine was described. The deaths from tetanus as the result of gelatine injection were of considerable frequency in Germany, where it was used for the arrest of hæmorrhage, suggesting that preventive measures were not carefully taken in the emergency. Certain researches were referred to which showed that commercial gelatine frequently contained tetanus germs, and that these could be destroyed by boiling the gelatine for ten minutes. Reference was also made to the disadvantage of the pyrexia sometimes caused, as he believed, by the introduction of a foreign proteid into the blood, and the risk of setting up clotting in other vessels that were diseased. He thought it a good method where surgical measures were not applicable.

Dr. F. HAWKINS alluded to one case in which he had seen the gelatine injection employed for an abdominal aneurysm. The injection was followed by a severe rigor, great collapse, and vomiting lasting for three days. The patient, however, recovered and returned to work, but he died after some five months. At the necropsy there was found some clot in the aneurysmal sac. It was yet to be seen whether patients lived longer after this treatment than after ordinary methods.

Dr. A. J. WHITING asked how soon after the first injection in the case that died from tetanus described by Dr. Maguire the first symptoms appeared, as the incubation period of tetanus was usually ten or twelve days ; and if it occurred under this, as he had understood, it might suggest the possibility that the spasms were not tetanus. He also asked whether boiling the gelatine to sterilise it altered its solidifying power.

Dr. MAGUIRE said that the onset of the first symptoms of tetanus in his case occurred about a week after the first injection. He thought he had read of a case of tetanus in which the incubation period was twenty-four hours. Boiling the gelatine did not seem to materially alter its solidifying power.

Dr. GUTHRIE RANKIN, in reply, said he had never seen any untoward effects from the method, such as serious pyrexia or the setting up of clotting in other vessels. In no case were there ever any symptoms to cause anxiety. He emphasised the obvious and almost immediate good effects occurring after the ordinary methods of treatment had been tried without good result.





A CASE  
OF  
MULTIPLE MYELOMA (MYELOMATOSIS) WITH  
BENCE-JONES PROTEIN IN THE URINE  
(MYELOPATHIC ALBUMOSURIA OF BRADSHAW,  
KAHLER'S DISEASE)  
AND A SUMMARY OF PUBLISHED CASES  
OF BENCE-JONES ALBUMOSURIA

BY  
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WITH A REPORT ON THE CHEMICAL PATHOLOGY

BY  
DR. R. HUTCHISON AND DR. J. J. R. MACLEOD

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THE patient, J. T—, aged 50, a stoker, came under my observation at the German Hospital in May, 1900, but I did not make the diagnosis of multiple myeloma until the following July, when I happened to examine the urine by the ordinary methods. From May to July the Bence-

Jones proteid<sup>1</sup> in the patient's urine had been frequently, at one time daily, measured by Esbach's albuminimeter, but had been entered in the notes as ordinary albumen. The daily amount of urine was found to be about 2000 c.c., and it contained about 7 per mille of the proteid. The reactions, as afterwards ascertained, were quite typical, just as those described by Bradshaw, Kühne, Bence-Jones, and others. The most characteristic are, I think, the following (that is, when the urine is acid<sup>2</sup>):—Coagulation of the proteid at a much lower temperature (about 58° C.) than ordinary albumen, more or less solution of the precipitate at a higher temperature (*e. g.* when the urine is boiled), and complete or almost complete solution on adding acetic acid to the boiling urine; after the precipitate has been partially re-dissolved by boiling, a characteristic re-precipitation should take place on allowing the urine to cool. What Dr. Bradshaw considered to be the spontaneous precipitation of the proteid in his case (noted also in some other cases) was likewise observed in the urine of the present case. The urine sometimes was turbid with this precipitate when quite freshly passed, and on these occasions, the reaction being always very acid, the turbidity could not be due to phosphates. Exact details in regard to the urine are contained in the following history of the case, which includes reports on the urine by Dr. R. Hutchison.

<sup>1</sup> On account of the contention by A. Magnus-Levy (Hoppe-Seyler's 'Zeit. f. phys. Chemie,' Strassburg, 1900, vol. xxx, p. 200) that the so-called Bence-Jones albumose is really an albumen, I have referred to it in this paper as Bence-Jones proteid. For the sake of brevity, however, I have sometimes spoken of "Bence-Jones albumosuria," when I meant to signify the presence of Bence-Jones proteid in the urine. It seems that precipitin experiments fail to solve this question of the nature of the Bence-Jones proteid. In fact, the so-called "biological method" fails to distinguish the Bence-Jones proteid from various other proteids of human origin (*vide* Rostoski, "Zur Kenntniss der Präcipitine," 'Verhandl. der Phys.-med. Gesellschaft, Würzburg,' 1902, vol. xxxv, pp. 30—32).

<sup>2</sup> The urine is nearly always acid in Bence-Jones albumosuria cases.

*Family history.*—Father died at sixty-four. Mother died at ninety-three. A married sister, fifty-nine years of age, has diabetes. To be sure of this latter point I obtained a specimen of her urine on January 25th, 1901; it was of specific gravity 1042, clear, pale, of acid reaction, containing 6 per cent. sugar and a trace of albumen, and giving a reddish coloration on the addition of perchloride of iron (Gerhardt's reaction). Of the patient's five children, four are living and healthy, and the other is said to have died from an accident.

*Patient's history.*—He was always a strong man, and never remembers being seriously ill previously to present complaint. As a young man he had gonorrhœa and a sore on the penis (the latter at about the age of twenty-three), but he cannot recollect having had secondary syphilis. There is no history of alcoholism.

The patient thinks his present illness commenced about the end of 1899. On December 26th, 1899, he first noticed a tingling sensation in the finger-tips of the right hand, and could not hold a knife. He then seemed to improve, but towards the end of February, 1900, tingling and loss of power were gradually coming on in both hands, and at about the same time he began to suffer from pains in the loins. In the first part of May his back began to bend; attention was drawn to his stooping attitude. The loss of power in his hands necessarily compelled him to give up active work, but in spite of resting he felt exhausted.

*Note on admission to the German Hospital* (May 18th, 1900).—The patient is a stout, heavily built man (weight 84½ kilogrammes), with a rather sallow complexion. His back is bent forward in walking, and his whole attitude and the way he holds his hands remind one somewhat of paralysis agitans. He complains of having very little power in his hands and fingers. His fingers are stiff and painful on movement, and are always slightly flexed at the metacarpo-phalangeal joints. He cannot voluntarily bend them so as to touch the ball of the thumb, and any attempt to bend them for him causes great pain. There

is a diffuse swelling of the backs of the hands, the puffy appearance of which is especially noticeable near the metacarpo-phalangeal joints. The hands are slightly tremulous, and are generally kept held up to his chest, as if that position were the most comfortable. The movements of the wrist and elbow-joints are free, but in regard to the shoulder-joints he experiences considerable difficulty in raising his arms so as to touch his head.

The area of cardiac dulness is slightly enlarged, and soft systolic murmurs are heard, attributable to the mitral and aortic valves. The lungs show nothing abnormal. There is a large, old, right inguinal hernia. Some pigmentation and scars on both shins are regarded by the patient as resulting from injuries at football. There is nothing special to note in regard to knee-jerks and cutaneous reflexes; there is no anæsthesia. The condition of the urine has already been alluded to, and more exact accounts will be given later on.

Under treatment, chiefly by rest, local hot baths, electricity, and slight massage, the condition of the hands seemed to improve somewhat, so that, when patient left the hospital on July 5th, 1900, he could bend his fingers sufficiently to touch the ball of the thumb.

The patient, after leaving the hospital, was seen from time to time. On July 16th, 1900, when he came up for examination, the kyphosis in the dorsal region was *very* noticeable. He had some difficulty in getting up from the sitting position, but could walk without the help of a stick. The pulse was 84, of moderate volume and tension. Respirations 26. Tongue slightly furred. On examining the abdomen the liver could be felt a little below the costal margin, but the upper limit of hepatic dulness appeared to be in about the natural position. The spleen was not felt. There was a little œdema in the lower part of the legs, but none at the loins. The handwriting was somewhat tremulous. About this time I thought there was evidence of wasting in the pectoralis major muscle on each side. The biceps muscles and the

thenar eminences likewise appeared relatively small. There was, however, no very marked muscular atrophy anywhere. Dr. F. E. Batten (July 18th, 1900), who kindly examined the patient, found the reaction to faradism in the muscles of the upper extremities and hands fairly good, but the current on that occasion was not strong enough to test the reactions to galvanism. He thought the patient's shoulders appeared thickened. Nothing abnormal was discovered in regard to sensation (for heat and cold, etc.). Knee-jerks active and equal. No ankle-clonus. Plantar reflexes natural. The patient at that time apparently suffered no pain, and there was no special tenderness on tapping any part of the cranium or vertebral column. The hot weather seemed to give the man greater freedom of movement. Later on (August) an ophthalmoscopic examination (one eye only) was made, but with negative results.

At the commencement of September Dr. Batten kindly made another electrical examination, and reported—"All the muscles of the arm and hand react to faradism, but they require a strong current in order to make them contract well. The muscles react badly to galvanism; it requires a strong current in order to get a contraction. There is very little difference between the KCC and ACC; the former appears, however, to be somewhat the stronger."

A blood examination on July 18th, for which I am indebted to Dr. Drysdale, gave the following results:—Red cells 3,214,000 in the cubic millimetre; total leucocytes 12,000; of the leucocytes the lymphocytes constituted 34·7 per cent., the large mononuclear 7·1 per cent., the polymorphonuclear 56·2 per cent., the eosinophile 2 per cent.; there were no myelocytes. Conclusions:—Slight leucocytosis; all forms proportionately increased; slight anæmia.

On July 12th, 1900, the nature of the proteid in the urine was first recognised. On this occasion a microscopic examination was made of the sediment collected by the centrifuge from a specimen of the urine which had

been allowed to stand for some time. It contained hyaline casts,<sup>1</sup> some of them sprinkled with granules or containing cells; also a few round cells and one or two oxalate of lime crystals.

From this time until the patient's death the urine was examined at various intervals, and was always found to give typical reactions for the Bence-Jones proteid. The specific gravity varied apparently from about 1012 to 1020. Sugar was tested for on different occasions, but with a negative result. No Gerhard's reaction (perchloride of iron test) was obtained. Sometimes the patient's urine, as already mentioned, was turbid when freshly passed,<sup>2</sup> evidently with what Dr. Bradshaw believes to be a spontaneous precipitate of the Bence-Jones proteid. This was notably the case when, at Dr. Bradshaw's suggestion, a few small doses of benzoate of ammonium had been previously given and the reaction of the urine was very acid. Dr. Bradshaw considers the spontaneous precipitate to be the proteid, because "when it has been separated out by the centrifuge and suspended in a little water, it is almost entirely dissolved by a little caustic soda and thrown down again by nitric acid."<sup>3</sup>

Dr. R. Hutchison kindly undertook a quantitative examination of the Bence-Jones proteid in the patient's urine. The urine passed during forty-eight hours (July 24th to 26th, 1900) was carefully collected and sent to him. His report is as follows:

<sup>1</sup> A later microscopical examination (August 9th, 1900) confirmed the presence of hyaline casts in the urine. On the other hand, Dr. R. Hutchison found casts absent in a specimen examined by him at the end of July, 1900.

<sup>2</sup> The spontaneous precipitate appeared sometimes to occur, not before the urine was passed, but soon afterwards.

<sup>3</sup> To find out more carefully whether a sediment consists entirely or partially of the Bence-Jones proteid, Dr. Bradshaw recommends the following:—"Draw it off with the pipette and reduce it to a small bulk on the centrifuge. Shake it up with water containing a trace of acetic acid (to dissolve any phosphates present), and centrifugalise again. This washing may be repeated. Collect the deposit on a filter and extract it with 0.2 per cent. caustic soda." The filtrate should give the usual reactions for the Bence-Jones proteid.

The urine was pale in colour, of specific gravity 1020, faintly acid in reaction, and somewhat more viscid than normal. There was sometimes a slight amorphous whitish deposit containing a few crystals of oxalate of lime. There were no casts.

The urine contained about 0.83 per cent. (estimated by precipitate with alcohol, drying and weighing) of a proteid which separated out in flocculi at a temperature of 58° C. On boiling, the precipitate disappeared, in some specimens entirely, reappearing on cooling; in others it gathered into a viscid mass which floated on the top.

Nitric acid gave a precipitate which disappeared partially on heating, and reappeared on cooling.

Strong HCl gave a distinct ring with the urine diluted 1 in 20 (Bradshaw's reaction).

Acetic acid alone gave no precipitate. On the addition of potassium ferrocyanide solution an immediate but not very abundant precipitate appeared.

The proteid separated out slowly on prolonged contact with NaCl in excess; NaCl + acetic acid caused a rapid separation.

In some specimens the proteid was precipitated by half-saturation with ammonium sulphate, in others only when the salt was added in slight excess.

No precipitate appeared on dropping the urine into an excess of distilled water, and it was only partially precipitated on prolonged dialysis.

On digestion with pepsin-HCl a considerable residue was left.

On an average about 15 grammes of the substance were excreted daily, and the urine contained no other proteid.

The total phosphates were estimated on two days with following results:

<i>Total P<sub>2</sub>O<sub>5</sub>.</i>	<i>Earthy P<sub>2</sub>O<sub>5</sub>.</i>
1. 1.173 grammes.	0.890 gramme.
2. 1.860 grammes.	

Dr. Hutchison added that the total of phosphates excreted was low, but the ratio of earthy to alkaline phosphates was high. He likewise collected some of the pure Bence-Jones proteid from the urine and found it to contain no phosphorus. In this respect, he pointed out, his results agreed with those in most previous cases.

I endeavoured on one occasion to find out whether an alteration in the diet of the patient would produce a corresponding alteration in the amount of the Bence-Jones proteid excreted in his urine. For two days (July 26th to 28th, 1900) the patient abstained from

meat, fish, and eggs, taking bread, butter, milk, and milk pudding. During the last twenty-four hours on this diet the patient passed 2100 c.c. of urine, which the rough test by Esbach's tube showed to contain 7 per mille proteid. Therefore the patient continued, in spite of the alteration in diet, to pass about 15 grammes of the Bence-Jones proteid in twenty-four hours.

The patient's general condition apparently remained stationary for a considerable time after leaving the hospital in July. Keeping the bowels open, and a saline diuretic medicine, seemed to suit him best. In December, however, he rapidly lost ground, and was re-admitted December 27th, 1900.

*Notes after re-admission.*—The patient has become much weaker, and has wasted much (weight on December 27th, 1900, 67½ kilogrammes). The loss of power in the upper extremities has remained about the same. The right arm can be moved more than the left one. There is marked wasting of supraspinatus, infraspinatus, and biceps muscles on each side, and there seems to be some enlargement of the head of each humerus. There is likewise an abnormal "tapering" of the fingers, and the fleshy cushions in front of the terminal phalanges appear somewhat shrivelled. There is a spotty pigmentation of the skin of the hands. No anæsthesia can be detected.

The patient says that four of his teeth were so loose that he removed them with his own hand two weeks before re-admission. After re-admission several other teeth were found to be loose, and the tongue was swollen and indented and ulcerated, the ulcers corresponding to irritating teeth. There was some bronchitis, with mucopurulent expectoration, and slight impairment of resonance at the base of one lung. Dyspnoea on slight exertion. Temperature never up to 100° F. The liver and spleen could not be felt. No ascites; no œdema of the lower extremities. Attached to one of the ribs on the right side of the back, about the level of the inferior angle of the scapula, a little hard, rounded projection, of about the



size of a large cherry, was noted, not painful or markedly tender on pressure. This was, I think, in the ordinary position for one of the projections which in some individuals can be seen marking out the angles of the ribs and the tendinous structures connected with them.

*Urine.*—During twenty-four hours (December 29th to 30th, 1900) patient passed 1300 c.c. of urine, of sp. gr. 1016, and neutral reaction, slightly turbid with phosphates; in this urine one or two casts were detected under the microscope. During the next twenty-four hours (December 30th and 31st) patient passed 1500 c.c. of urine, of sp. gr. 1016, neutral in reaction, clear, and apparently free from casts. Gerhardt's reaction (with perchloride of iron) was negative on both days. The urine from these two days was sent to Dr. R. Hutchison, who kindly examined it, and found that it resembled the previous specimens:—"It gives all the reactions of Bence-Jones proteid, as set forth by Magnus-Levy.<sup>1</sup> In addition, it gives Bradshaw's hydrochloric acid reaction quite distinctly. The patient is excreting about 16 grammes of the substance daily, and about 1·5 grammes of  $P_2O_5$ ."

Patient's teeth were attended to and some loose ones removed. The ulcers over the front of the tongue (local treatment by chromic acid solution, etc.) apparently got better, but there was a bad one at the back, and the tongue felt hard and infiltrated. The lingual condition then seemed to be gummatous, as Dr. Bradshaw suggested when he saw the case. Iodide of potassium was accordingly prescribed, and quinine was likewise given. Under this treatment the condition of the tongue apparently improved somewhat. The pulse was generally between 90 and 100, and respiration between 30 and 36.

On the evening of January 24th, 1901, severe hæmorrhage from the bowel occurred, causing a state of collapse. With camphor hypodermics and inhalation of oxygen

<sup>1</sup> Loc. cit.

there was temporary improvement, but on the evening of January 25th patient died quietly.

An examination of the blood kindly made by Dr. Drysdale on January 21st, 1901, had given the following results:—Hæmoglobin, 23 per cent. of the normal; red cells, 2,980,000 in the cubic millimetre; total number of leucocytes, 11,000; of the leucocytes, the lymphocytes constituted 25·6 per cent., the large mononuclear 3 per cent., the polymorphonuclear 70·3 per cent., the eosinophile 1 per cent.; there were no myelocytes or atypical cells seen in 300 leucocytes counted. Conclusions: slight leucocytosis; no special change. Dr. Drysdale added that owing to running over in von Fleischl's apparatus the hæmoglobin was possibly estimated at slightly too low a value.

#### NECROPSY AND PATHOLOGICAL EXAMINATION.

The necropsy was performed on January 26th, 1901, about sixteen hours after death. For convenience I shall arrange the results of the whole pathological investigation under the following headings:

1. The mouth and alimentary canal.
2. The other abdominal viscera.
3. The thoracic viscera, etc.
4. The nervous system and muscles.
5. The joints, tendons, etc.
6. The skeleton and myelomatous growth.
7. The chemical examination by Drs. Hutchison and Macleod.

##### *1. The Mouth and Alimentary Canal.*

The tongue was ulcerated and hardened, apparently from a diffuse inflammatory infiltration or from new growth. Microscopic examination showed the presence of a diffuse gummatous change. It is perhaps worthy of

remark that in sections of the tongue stained with methyl violet a good deal of amyloid (lardaceous) or closely allied substance<sup>1</sup> was found, though none was discovered in similarly stained sections of the liver, spleen, and kidney. In an article on "Syphilis and Lardaceous Disease"<sup>2</sup> in 1895 I drew attention to the occasional localisation of amyloid changes about syphilitic gummata.

Nothing noteworthy was observed in the stomach, but there was a rather deep chronic ulcer in the duodenum close to the pylorus, and this was doubtless the source of the blood passed from the bowels during life. The intestines contained blackish material, the colour doubtless being due to altered blood.

## 2. *The other Abdominal Viscera.*

The *liver* was rather large, weighing 78 ounces, but its substance neither macroscopically nor microscopically showed anything noteworthy. The *gall-bladder* contained green bile. There were no gall-stones. The *pancreas* showed nothing abnormal. The *spleen* weighed about six ounces; sections under the microscope showed the presence of a good deal of pigment.

The *kidneys* looked rather pale, but it must be noted that most of the organs appeared somewhat bloodless, doubtless owing to the poorness of the blood in hæmoglobin and to the profuse intestinal hæmorrhage preceding death. Both kidneys together weighed about twelve ounces. The capsules were partially adherent, the cortex had a slightly granular surface, and there were one or two cysts. Under the microscope a moderate amount of fibrotic change (chronic interstitial nephritis) was ob-

<sup>1</sup> If the substance in question was not actually amyloid, it was a very closely allied body, as the rosy coloration with methyl violet proved. It was certainly much nearer to amyloid than to hyaline substance. The muscular coats of the small blood-vessels were, however, as yet not quite characteristically picked out.

<sup>2</sup> 'American Journ. Med. Sciences,' November, 1895.

served, explaining the presence of hyaline casts in the urine during life.

The *adrenals* appeared normal. The *mesenteric glands* were not specially large. No chalky deposits were discovered in the kidneys or other organs, such as Virchow has described ('Kalk-Metastasen') in cases where bony tissue has been rapidly destroyed by malignant neoplasms, and such as were found in the kidneys in Stockvis's case of multiple myeloma with Bence-Jones proteid in the urine (see Case No. 4 in the summary). A few such were noted in my case of multiple myeloma examined in 1897, which in some respects clinically resembled the present case, though there was probably no Bence-Jones proteid in the urine.<sup>1</sup> It must be remembered, however, that in the last-mentioned case the bone had been destroyed more rapidly and to a much greater extent than in the present case. Moreover, some of the microscopic calculi were situated in the neighbourhood of minute cystic adenomata of the kidney, and I have reason to believe that they may accompany renal adenomata in persons who are quite free from any bone disease. Very similar bodies were mentioned by Charles Sabourin in his well-known paper on multiple adenomata in cirrhotic kidneys,<sup>2</sup> and they were present likewise in the case of "papillary adenoma of the kidney" which I recorded in

<sup>1</sup> 'Transactions of the Pathological Society of London,' 1897, vol. xlviii, p. 169; and 'Journal of Pathology,' January, 1898. I shall have to refer to this case later on in greater detail. Only one entry on the urine could be found in the notes. It said that there was "no albumen." The house physician who examined the urine might just possibly have overlooked the presence of Bence-Jones proteid, as in testing for albumen he frequently used only the potassium ferrocyanide and acetic acid test, and Dr. Bradshaw, using this test in his case, found that no turbidity was produced at first unless a large excess of the acid was added, though after several minutes the turbidity gradually appeared. Judging, however, from the reaction in J. T.—'s urine, which was fairly rapid to the ferrocyanide test, I think it very unlikely that any such mistake occurred.

<sup>2</sup> 'Revue de Médecine,' Paris, 1884, p. 446.

the 'Transactions of the Pathological Society of London,' 1898.<sup>1</sup>

### 3. *The Thoracic Viscera, etc.*

The *heart* weighed thirteen ounces. The inner surface of the left auricle was hard and very rough, evidently the result of a former extensive endocarditis. The mitral, aortic, and pulmonary valves were not diseased, but there was some irregular thickening of the tricuspid valve. The *pericardium* contained about two ounces of clear serous fluid. There was much atheroma of the *thoracic aorta*. There was evidence of *bronchitis*, and portions of the lung substance appeared collapsed. There was no pleuritic effusion. Some pigmented and moderately enlarged *mediastinal glands* were observed. The *thyroid gland* macroscopically and microscopically showed nothing abnormal.

### 4. *The Nervous System and Muscles.*

The brain weighed about fifty-four ounces. The membranes were slightly thickened. Dr. F. E. Batten kindly undertook the examination of the brain, spinal cord, a part of the left brachial plexus, and the nerves and muscles of the right hand, that in which the loss of power and tremor had been most marked during life. Following is Dr. Batten's report:

"The brain and spinal cord were examined by the Nissl, Marchi, Weigert-Pal, and van Gieson methods. Nothing abnormal could be detected except that the cells of the anterior horns contain an abnormally large amount of pigment granules.

"*The peripheral nerves.*—With regard to the peripheral nerves, nothing abnormal could be detected either in the ulnar, radial, or median nerves, either in section or in the teased specimens.

<sup>1</sup> Vol. xlix, p. 177.

"*Muscles.*—The small muscles of the hand examined were the abductor minimi digiti and the abductor pollicis. By the Marchi method the muscle-fibres appear to be normal both on longitudinal and transverse section. By the van Gieson method the greater part of the muscle appears to be normal; in one bundle, however, there is an increase of the nuclei of the sheath of the fibres. The fibres themselves are about the natural size, and their transverse striation is normal."

#### 5. *The Joints, Tendons, etc.*

One hip-joint and one shoulder-joint were examined, and showed no destruction of articular cartilage, but showed a certain amount of "lipping," much capsular thickening, and excessive villous growth and formation of pendulous bodies from the synovial membrane. The wrist-joint and the metacarpo-phalangeal joints of the right side were likewise examined; they showed similar alterations. In some of them synovial fringes projected between the opposing articular cartilages, partially separating them from each other. The whole condition resembled one of rheumatoid arthritis. The lump noted during life on the posterior portion of one of the ribs was examined and found to be an early gummatous formation in the tendinous structures at one of the costal angles.

#### 6. *The Skeleton and Myelomatous Growth.*

The vertebral centra, the ribs, the sternum, part of the skull, and some of the bones of the extremities were examined. The bone-marrow and cancellous tissue were found more or less uniformly infiltrated by tumour growth. It is not too much to say that the whole skeleton was more or less involved, even the diploë of the skull and the marrow of the terminal phalanges of the fingers. The softening and yielding of some of the dorsal vertebræ, consequent on the tumour formation, were the cause of

the progressive kyphosis noted during the patient's life. The body of one of the vertebræ was so altered in shape that in a sagittal section it appeared as a triangle with its apex towards the front of the body, wedged in between two centra which might comparatively be said to have retained their normal shape. In some parts the bone-marrow and cancellous tissue seemed to have completely given place to the new growth. Thus, much of the interior of the manubrium sterni was occupied by a soft tumour mass from which all bony matter had disappeared. Nowhere, however, even in the ribs and sternum, had the tumour given rise to any external protuberances, such as have been recorded in some cases of multiple myeloma; and nowhere had it led to the occurrence of fractures. On the whole, far less absorption of bony substance had taken place than in my case of multiple myeloma (without Bence-Jones proteid in the urine) examined in 1897.<sup>1</sup> In that case the ribs had been converted into thin-walled tubes filled with soft growth, and in some places the periosteum and bony shell had been bulged out by the tumour; many spontaneous fractures had occurred, and one of the vertebral centra was almost entirely replaced by diffuent new growth.

In the present case, as in the case just alluded to, the new growth seems to have commenced in different parts at the same time, and it is impossible to pick out any portion of the tumour as being the primary growth. If the tumour be termed myeloma the whole process may, for this reason, justly be termed "myelomatosis."

Some portions of the growth are quite pale, others deep red. This redness of certain portions is seen by microscopic examination to be due to a large amount of blood not contained in blood-vessels, but lying free amongst the tumour cells.

The growth consists chiefly of mononuclear rounded or polyhedral cells, the characteristic of which, by the ordinary methods of staining, is that many of them are

<sup>1</sup> 'Trans. Path. Soc.,' loc. cit.

crammed full of globules, and that these globules stain with eosine almost exactly like red blood-corpuscles. They seem, indeed, at first sight to be red blood-corpuscles included in the tumour cells, though they vary greatly in size, some being much larger and some smaller than ordinary red cells. But, on examining specially stained preparations, another explanation of the appearance, one suggested to me by Professor R. Muir, of Glasgow, becomes far more probable. He has examined the growth and has kindly sent me a report, which I shall now quote :

"I have examined the tissue carefully, after staining in various ways, and have come to the following conclusions:—It may be said to have the general characters of a sarcoma, and its vessels resemble more closely those of a sarcoma than those of the marrow. It is composed of practically one variety of rounded cell, which presents certain resemblances to the neutrophile myelocyte, from which, however, it differs in the relatively smaller size of the nucleus and in the more abundant protoplasm. In the protoplasm, moreover, there can be shown a large number of granules which vary considerably in size, but the smallest and most abundant of which are distinctly larger than the neutrophile granules. With hæmatoxylin and eosine these smallest granules are practically unstained by the eosine; with Ehrlich's tri-acid they are coloured, but have not quite the same tints as the neutrophiles, the staining being of a dirty brown colour; with Mann's eosine-methyl-blue combination<sup>1</sup> they are stained

<sup>1</sup> Dr. Gustav Mann's stain was first published in 'Proceedings Scottish Microscop. Society,' 1893-4, p. 165. The method is likewise described in full in a paper by Copeman and Mann on the "Histology of Vaccinia" ('Annual Report of the Medical Officer of the Local Government Board,' 1898-9, p. 509).—The description is as follows :

*"Mann's Bi-acid Mixture of Methyl Blue and Eosine."*

"1 per cent. methyl blue in distilled water	. 35 c.c.
1 per cent. eosine in distilled water	. 45 c.c.
Distilled water	. 100 c.c.

"Sections are left in this mixture for five to ten minutes, washed in



bright red with a slightly violet tint (whereas the neutrophiles are unstained) ; with Unna's polychrome methylene blue the granularity is faintly visible, but the granules are not really stained. We may therefore say that they have, on the whole, a more distinctly (though not a pure) oxyphile reaction than the neutrophile granules. Only a very small proportion of the cells appear to be without granules. In addition, however, to these small granules, many larger ones are present, and all intermediate sizes can be found up to large rounded bodies as large as, or even larger than, ordinary red corpuscles. I thought at first that these rounded bodies were included red corpuscles, but, on more careful examination, I believe that they are formed by the confluence of smaller globules. Some of them also are seen lying free. They are more distinctly oxyphile than the smaller granules, and stain with eosin by the ordinary methods. It is also to be noted that the rounded bodies lying free stain with the tri-acid stain of a different tint from the red corpuscles ; further, they always seem to be

water, dehydrated, and mounted in balsam. This constitutes what may be termed the 'short method.' Or they are dealt with by the 'long method,' i.e. are left in the stain twelve to twenty-four hours, then washed in distilled water, thoroughly dehydrated, and placed in a vessel containing absolute alcohol 30 c.c., to which previously five drops of a 1 per cent. solution of KHO in absolute alcohol have been added. When the sections have turned a reddish tint, the slide is washed with absolute alcohol to remove the alkaline alcohol, then rinsed in distilled water till differentiated. If the sections are not blue enough, a drop of acetic acid added to the water in which they are being rinsed will restore the colour."

Professor Muir used Mann's long method without any other stain afterwards. Some sections stained by Ehrlich's acid hæmatoxylin after Mann's long method gave the large globules in the tumour-cells a slightly different tint. When the sections had been stained according to the preceding directions, they were passed through water into Ehrlich's acid hæmatoxylin, and after having been kept there from one half to two minutes, they were washed in tap water, dehydrated, and mounted in the usual way. For preparing sections from this case, and from two other cases of myelogenic growth, I am much indebted to Mr. E. H. Shaw.

perfectly spherical in form. I should also have mentioned that in the tumour-cells there is often a narrow zone around the nucleus which is comparatively free from granules.

"I accordingly consider that the tumour is formed by a special and characteristic type of cell, which is probably derived either from the neutrophile myelocyte or its predecessor; that this cell produces in its protoplasm in a granular form a substance which is closely allied to, though not quite identical with, the substance of the neutrophile granules; and that this substance is formed in excess, and may form larger granules by confluence of the smaller, the larger globules sometimes becoming free."

According to J. H. Wright's report on a case examined by him,<sup>1</sup> the principal tumour-cells in the case in question appeared to be a variety of Unna's "plasma-cells." Dr. J. M. H. MacLeod has kindly examined sections from the present case to compare the cells with Unna's plasma-cells. He has used the special methods of staining for this purpose, and tells me:—"Morphologically the cells resemble plasma-cells in that they are polyhedral and their nucleus is placed excentrically. The nuclei, however, do not show the characteristic arrangement so generally found in plasma-cells of five or six deeply stained chromatin bodies around the periphery."

Since receiving Professor Muir's report I have examined a number of sections from the sternum stained by Mann's method and by Ehrlich's tri-acid stain (see Plate IV). There is a sprinkling of small cells, resembling lymphocytes, with round nucleus and little protoplasm; but with this exception the growth is practically composed of the same kind of cells as those mentioned as characteristic in the parts from which Professor Muir made his report. Some of the larger globules referred to by Professor Muir are two or three times as large as ordinary red corpuscles, and a good number of

<sup>1</sup> 'Johns Hopkins Hospital Reports,' 1900, vol. ix, pp. 359-366. (See Case No. 13 in the summary of cases at the end of the present paper.)

them are free, lying singly or in groups amongst the tumour-cells. The globules of about the same size as red corpuscles are, however, more numerous, and are mostly enclosed in tumour-cells or arranged in clusters as if those of each cluster had been formed in a single cell and were still united together in some way. Such clusters often consist of a dozen or more globules, and sometimes resemble mulberries or bunches of grapes.

By Mann's method the *globules* in question are not all stained exactly alike. Sometimes they are stained quite like the red blood-corpuscles are, but generally they take on a distinctly more violet or brownish-violet colour, and this is especially the case in sections which I had stained with Ehrlich's acid hæmatoxylin<sup>1</sup> after Mann's eosin and methyl-blue combination. On the other hand, the *smaller granules* are less well stained when the sections are treated for shorter lengths of time in the alkaline alcohol, when acetic acid is not used and when hæmatoxylin is likewise employed.

Red corpuscles (taking on the eosin stain), if they were included in the tumour-cells (stained blue), would also appear violet in colour, and in some pathological conditions the red corpuscles vary greatly in size and do not all stain alike. The globules in the present tumour tissue are, however, distinguished from red corpuscles not only by their great variation in size and by their reactions to special stains, but also by their being spherical in shape. Moreover they are, if anything, best seen in the paler parts of the growth, where there are fewer red blood-corpuscles.

We may conclude that the granules and globules of different sizes, which constitute a characteristic feature of the tumour-cells in the present case, are probably all of the same nature, though they vary almost as much in size as do fat globules<sup>2</sup> in a fatty liver. Some of the tumour-

<sup>1</sup> See the foot-note about Mann's stain.

<sup>2</sup> In fact, if it were not for their reactions, one might suppose that all these globules were fat. Owing, however, to the method employed in

cells appear tightly packed with medium-sized globules, others contain one or two larger globules, quite three times as large as ordinary red blood-corpuscles. A good many of the larger globules can be seen lying free amongst the tumour-cells, as if they had been cast off or had been set free by the disintegration of the cell in which they were originally found.

At the end of his report Professor Muir suggested a possible relationship between the granule and globule formation in the tumour-cells and the excretion of Bence-Jones proteid in the urine. The view that the globules may represent a stage in the formation of the proteid in question is supported by the consideration that during the life of the patient these globules were probably being produced in *all* the bones of his body. Further investigation in other cases will doubtless throw more light on the question. If, however, these globules are in any way connected with the Bence-Jones albumosuria, why have they not been discovered in the microscopical preparations from other cases? It is, perhaps, worth mentioning that in the present case the tissues were at once put into weak formalin, where some of them were kept for several months before sections were cut.<sup>1</sup>

7. *The Chemical Examination by Drs. R. Hutchison and J. J. R. Macleod.*

For examination they had—

- a. Blood and clots from heart, etc.
- b. Clear serous fluid from pericardium.

preparing the sections (embedding in paraffin), all true fat would have been dissolved out. Professor Muir tells me that the granules in the growth may possibly be chemically related to vitelline granules, and he thinks that their staining reactions correspond with those of the zymogen granules of the pancreas, but he has stated in his report what he believes to be the most probable source of such granules in the marrow.

<sup>1</sup> A 4 per cent. aqueous solution of formalin slowly precipitates the Bence-Jones proteid from the urine.

c. Parts of ribs, spinal column, and long bones.

d. Parts of liver, spleen, kidneys, and striped muscle.

In their report they at first recapitulate the chemical reactions of the proteid in the patient's urine, and then give an account of their chemical examination of the tissues obtained at the necropsy.

#### THE CHEMICAL REACTIONS OF THE BODY IN THE URINE.

Several samples of the urine were furnished us, in which we employed most of the reactions described by previous writers.<sup>1</sup> The following were the chief results obtained :

1. *Heat coagulation*.—A coagulum appeared at about 58° C. In one of the samples this coagulum disappeared entirely on boiling, returning on cooling. In two other samples, however, the coagulum did not clear up entirely on boiling, but the diffuse coagulum collected itself into flocculi on the surface of the liquid.

2. *Nitric acid*.—The addition of 25 per cent. nitric acid produced a coagulum which cleared up partially on boiling, becoming again more distinct on cooling. By employing Heller's method a sharp ring was obtained, which became less distinct on carefully warming the test-tube.

3. *Hydrochloric acid*.—This was employed by the method described by Bradshaw (namely, pouring the urine diluted twenty times on to the surface of the acid), and a very distinct ring was obtained.

4. *Potassium ferrocyanide and acetic acid*.—A slight precipitate was obtained, which became less distinct on boiling.

5. *Saturation with common salt and the addition of acetic acid*.—A rapid and abundant precipitate was produced.

6. *Half-saturation with ammonium sulphate*.—In one sample this produced complete precipitation of the body, the filtrate being proteid-free. In two samples, however, this amount of the salt did not effect complete precipitation, a much larger quantity being necessary to produce that result. The addition of two volumes of a saturated solution of ammonium sulphate produced complete precipitation. This precipitate was collected on a filter-paper, washed

<sup>1</sup> Bence-Jones, 'Philosoph. Transact. Roy. Soc.,' 1848, part 1, p. 55; Hüppert, 'Prager med. Wochenschr.,' 1889, S. 35; Kühne, 'Zeitschrift f. Biolog.,' 1883, Bd. xix, S. 209; Matthes, 'Verh. d. 14 Congresses f. innere Medicin,' 1896, S. 476; Ellinger, 'Deut. Arch. f. klin. Med.,' 1899, Bd. lxi, S. 255; T. R. Bradshaw, 'Med.-Chir. Trans.,' vol. lxxxi, p. 259; Kalischer, 'Deut. med. Wochenschr.,' 1901, S. 54.

with a saturated solution of ammonium sulphate, and dissolved by adding water. The resulting solution was dialysed for several days. The dialysate was slightly opalescent and gave the following reactions:

On heating, a coagulum was obtained at 66° C., which cleared up entirely at 90° C. After the addition of one drop of 20 per cent. acetic acid to 20 c.c. of the fluid, the coagulum appeared at 50° C., and also cleared up at 90° C. Nitric and hydrochloric acid tests as above. Two volumes of saturated common salt solution with a few drops of acetic acid gave a copious precipitate. Acetic acid and potassium ferrocyanide gave a precipitate which cleared up considerably on heating. On boiling for some time with hydrochloric acid a distinct violet colour was produced, which was probably due to some chromogens present in the dialysate. Boiling with nitric acid did not produce this effect.

7. *Alcohol*.—Complete precipitation was produced by adding 2 vols. 96 per cent. alcohol. The precipitate was soluble in weak ammonia.

8. *Acetic acid*.—No precipitate.

9. *Neutralisation with sodium hydrate or ammonia*.—No precipitate.

10. *Neutralisation with caustic soda after strongly acidifying with acetic acid*.—No distinct precipitate.

11. No precipitate was produced by dropping the urine into an excess of distilled water.

12. A sample of urine was dialysed for several days. There was a slight precipitate, which was not proteid in nature. The dialysate gave all the above reactions.

From a consideration of the above results it is evident that the case was a typical one of Bence-Jones albumosuria. No albuminuria was present, as the urine was rendered proteid-free by the addition of twice its volume of a saturated solution of ammonium sulphate. No globulin was present, since no proteid separated out from the urine on dialysis. The precipitate obtained by the addition of 2 vols. saturated ammonium sulphate solution was dissolved by adding water, and was then subjected to dialysis for several days. After this it was reprecipitated in the dialysate by the addition of alcohol; the precipitate was filtered off, washed several times with alcohol, and tested for phosphorus (after fusion in a silver basin with salt-petre and caustic soda), with a negative result. This proves the absence of nucleo-proteid.

## THE CHEMICAL EXAMINATION OF THE ORGANS.

Up to the present time only three cases have been recorded in which a chemical investigation of the organs was made.

The first of these is by Ellinger,<sup>1</sup> but the clinical history of the case shows it to have been of an unusually acute nature, and the symptoms scarcely typical of myelogenous disease.

The tissues examined were a piece of infiltrated rib, blood, and some ascitic fluid.

In the case of the piece of rib, the following somewhat rough method was employed. The piece of rib was macerated with water, the resulting extract was filtered off, and to part of it was added some sodium chloride and acetic acid, whereby a precipitate was produced. In another part of the watery extract the point of heat coagulation was determined and found to be 40° C.

The author mentions that a piece of normal rib-marrow treated in the same way does not give these reactions.

In the case of the blood and ascitic fluid, a more reliable method was employed.

To each was added an excess of alcohol, and the resulting precipitate was allowed to stand several days. It was then filtered off and macerated with water. The resulting watery extract was then weakly acidified with acetic acid and boiled. The boiling fluid was quickly filtered, so as to separate all coagulated proteid, and the filtrate, at first quite clear, gradually became cloudy on cooling, and gave the reactions for Bence-Jones proteid.

The second case is recorded by Askanazy,<sup>2</sup> and is peculiar in that an examination of the blood during life, and of the lymphatic glands after death, showed it to be one of lymphatic leukaemia.

The tissues examined were marrow from the vertebrae and head of femur, lymphatic tumours, blood, pericardial and pleuritic fluids.

Two methods were employed in testing for the proteid. One of these consisted in making a watery or weak caustic soda extract of the tissue. This was then treated with acetic acid, so as to precipitate nucleo-proteid, which was filtered off. In the filtrate the heat-coagulation point was determined. It was then boiled and filtered hot, the resulting filtrate being gradually cooled. The other method consisted in adding alcohol to the extract, collecting the precipitate, and macerating it with weak caustic alkali. The resulting extract

<sup>1</sup> 'Deut. Arch. f. klin. Medicin,' 1899, Bd. lxii, S. 255. (See Case No. 9 in the Summary.)

<sup>2</sup> Ibid., 1900, Bd. lxxiii, S. 34. (See Case No. 16 in the Summary.)

was then treated with acetic acid to precipitate nucleo-proteid, and to the filtrate from this were applied the tests for Bence-Jones proteids.

By means of these methods it was found that the Bence-Jones proteid was present in the marrow, but absent from the lymphatic tumours, blood, and pericardial and pleuritic fluids.

The alcohol method was employed in a sample of urine containing the albumose, and was found to give reliable results.

The third case is that of Kalischer,<sup>1</sup> and the tissues examined were marrow from the ribs and humerus. The examination was made by Prof. Löwy, but he could not find a trace of Bence-Jones proteid.

*Methods employed in the present case.*—In the present case a very complete chemical investigation was possible, as we were fortunate in securing not only portions of all the organs, but also large quantities of bone from various regions.

Two methods, very similar to those described by Magnus-Levy, were employed to detect the body.

The bones were crushed into fragments in a quartz crusher, the other tissues being chopped up into small pieces. Each was then ground up in a mortar with distilled water, and the resulting pulp allowed to stand twenty-four hours. The extract was filtered off, and the remainder again pounded in the mortar with distilled water, the second extract, after filtration, being added to the first

The resulting watery extract from each tissue was then carefully neutralised and divided into two equal parts. To one of these were added two volumes of a saturated solution of ammonium sulphate, and the mixture allowed to stand twenty-four hours. The resulting precipitate was separated by filtration, washed with ammonium sulphate solution, and suspended in water. After standing several days this suspension was filtered, and the filtrate placed in a parchment dialyser, for several days in running water, and finally for at least two days in distilled water, which was frequently changed. After dialysis, a precipitate invariably separated out (globulin), which was removed by filtration. The resulting filtrate was tested for Bence-Jones proteid. To the *second* portion of the neutralised watery extract twice its volume of spirit was added, and the mixture was then boiled (by which means the native proteids become coagulated, whereas the Bence-Jones proteid does not).<sup>2</sup> The mixture was then filtered, and the precipitate, after being washed with

<sup>1</sup> 'Deutsch. med. Wochenschr.,' 1901, No. 4, S. 54. (See Case No. 22 in the Summary.)

<sup>2</sup> Magnus-Levy, Hoppe-Seyler's 'Zeit. f. phys. Chemie,' 1900, Bd. xxx, S. 200.



boiling 66 per cent. spirit, was suspended in  $\frac{1}{2}$  to  $\frac{1}{3}$  per cent. ammonia, and either left in this for several hours or heated on the water-bath (by either of which processes a solution of the albumose results, while the coagulated proteids remain unaffected).

The former of these methods we will designate the ammonium sulphate method, the latter the alcohol method.

These two methods were applied to urine containing the substance in question. The resulting solutions gave the chief reactions for Bence-Jones proteid (see first part of report).

To serve as controls we also examined, by both methods, red marrow from the vertebræ of a healthy person, and by the ammonium sulphate method, red marrow from the ribs of a horse. *In neither of these was any trace of Bence-Jones proteid<sup>1</sup> found.*

*Results.*—The following are the results obtained from the various organs and tissues:

*Marrow of Bones.*—The marrow contained in these was apparently of two types—namely, a pink pasty mass in the head and lower extremity of the femur and in the ribs, and a thin red-currant-jelly-like mass in the shaft of the femur. We therefore divided the bones into three groups, viz. (1) vertebræ and ends of femur; (2) ribs; and (3) shaft of femur.

1. *Vertebræ and ends of femur.*—The neutralised extract by the alcohol method was very opalescent, and could not be cleared by filtration. It was accordingly dialysed for three days in tap water, and for twenty-four hours in distilled water. A slight precipitate separated out, and on filtration a clear solution was obtained. In the dialysates by both methods the following reactions were obtained:

*Heat coagulation.*—A coagulum was obtained at 70° C., which did not clear up on boiling. On filtering the boiling fluid, the filtrate did not show any opacity on cooling. On the addition of one drop 20 per cent. of acetic acid to 30 c.c. of the fluid, coagulation occurred at 50° C., but the precipitate did not clear up on boiling, although it appeared to do so to a certain extent because of the coagulum separating out as flocculi on the surface.

*Hydrochloric acid.*—A distinct sharp ring was obtained.

*Nitric acid.*—A similar ring was obtained, which cleared up considerably on heating, reappearing on cooling.

<sup>1</sup> In the case of the red marrow from the horse's rib, the extract by the ammon. sulph. method contained a trace of albumen coagulating at 75° C. In the case of the human vertebræ by the alcohol method, the application of the nitric and hydrochloric acid tests produced an indefinite haze but no distinct ring, and no coagulation occurred on heating even to boiling temperature.

Two volumes of a *saturated solution of common salt and a few drops 20 per cent. acetic acid.*—A precipitate.

A few drops *acetic acid and potassium ferrocyanide.*—A precipitate, not clearing on boiling.

*Biuret test.*—Violet reaction.

In the opalescent solution by the alcohol method the addition of one drop 20 per cent. acetic acid produced a precipitate, soluble, however, in excess of the acid.

2. *Ribs.*—By the alcohol method an opalescent fluid was obtained, which gave a very distinct precipitate on the addition of acetic acid. The opalescent fluid was dialysed for several days and filtered.

The clear fluid by both methods gave the following reactions:

*Heat coagulation.*—Slight haze at 60° C., which did not clear up on boiling.

*Nitric and hydrochloric acids.*—A distinct ring was obtained with both of these reagents, which cleared up considerably on boiling, becoming more distinct on cooling. A slight haze was produced by adding 1 in 10 HCl to the fluid.

*Acetic acid 20 per cent.*—A few drops of this produced a distinct precipitate insoluble in excess.

*Biuret test.*—Slight violet reaction.

The precipitate produced in the undialysed opalescent solution by the alcohol method on the addition of acetic acid<sup>1</sup> was fused in a silver basin with caustic soda and saltpetre; the resulting mass was dissolved in water, acidified with nitric acid, and mixed at 60° C. with ammonium molybdate solution. No trace of phosphorus was found present.

3. *Shaft of femur.*—The extracts contained only the merest trace of a proteid, and the only reactions which gave anything were the ring tests.

4. *Kidneys.*—Slight rings were obtained with the acids, and on boiling the fluid became opalescent.

5. *Liver.*—No trace of proteid was shown by any reaction by either method.

6. *Spleen.*—Same result.

7. *Muscle.*—Same result.

8. *Pericardial fluid.*—Slight rings were obtained with the acids, and on boiling an opalescence was produced. Acetic acid produced no haze. The ammonium sulphate method was alone employed, as only 45 c.c. of the fluid was examined.

9. *Bile.*—No trace of proteid.

<sup>1</sup> The amount of precipitate used for this test was quite sufficient for the purpose.

10. *Blood*.—55 grammes of clotted blood from the heart was examined. This was extracted with water, and the extract examined by both methods. In neither case was the slightest trace of proteid obtained.

*Consideration of results*.—From an examination of these results it will be seen that in no organ or tissue could the presence of a proteid identical with that found by the same methods in the urine be demonstrated. In the case of the vertebræ and ends of the femur, however, a *proteid giving very similar reactions* was obtained. It will be noticed that the points wherein this differs most from the typical Bence-Jones proteid are the temperature at which it coagulates, and the fact that it does not clear up on boiling. It will also be noticed that after the addition of the merest trace of acetic acid the point of heat coagulation was the same as that in a similarly treated extract from urine, but whereas the urinary coagulum cleared up at 90° C., that of the marrow did not do so, even on boiling.

Recent work by K. Spiro,<sup>1</sup> Hammarsten,<sup>2</sup> and others shows, however, that not only does the exact point of heat coagulation vary considerably with the dilution and composition of the fluid, but also that re-solution of the coagulum depends to a very large extent on the composition of the fluid in which it is suspended.<sup>3</sup> In view of these facts it is impossible to draw any deductions as to the nature of the body from a consideration of the heat-coagulation point alone, and the mere fact that any proteid whatsoever should have been obtained after the processes to which the original extract was subjected shows in itself *that some unusual proteid existed in the tissues*.

Nor could such a proteid be obtained by employing exactly the same methods from normal red bone-marrow.

The neutralised opalescent solution obtained by the alcohol method gave a copious precipitate on weakly acidifying with acetic acid. This precipitate was soluble in excess of the acid. It was easily soluble in weak alkalies and gave the xantho-proteid and other reactions for proteids. This precipitate was not present in the dialysate obtained by the ammonium sulphate method. From its reactions

<sup>1</sup> Hoppe-Seyler's 'Zeit. f. phys. Chemie,' 1900, Bd. xxx, S. 182.

<sup>2</sup> Pfüger's 'Arch. f. d. ges. Physiologie,' 1878, Bd. xviii, S. 65.

<sup>3</sup> It was noticed, both in the case of the urine and of the vertebral marrow, that, on allowing the extract to stand for four weeks in a stoppered bottle, a sediment had settled down. This was filtered off, and the clear filtrate failed to give any reaction for proteids. The precipitate was insoluble in weak alkalies. The albumose-like body had evidently undergone a change on standing. There was unfortunately not sufficient material to re-investigate this fact.

it would appear to be either an alkali-albumen or a nucleo-proteid. To decide this question it was tested for phosphorus, with a negative result. It is probable, therefore, that a certain amount of alkali-albumen had been produced out of the alcohol coagula by boiling with dilute ammonia. After the separation of this by neutralisation and dialysis, a clear solution giving exactly the same reactions as the ammonium sulphate extracts was obtained.

The extract obtained from the red-currant-jelly-like marrow found in the shaft of the femur contained only the minutest trace of proteid.

The only other tissue from which a proteid-containing extract could be obtained was the kidney, and here only in the minutest trace. The pericardial fluid gave rather clearer reactions than the kidneys, a result in accordance with Ellinger's observations.

#### CONCLUSIONS REGARDING THE SEAT OF PRODUCTION OF BENCE-JONES PROTEID.

The invariable, or almost invariable occurrence of bone-marrow disease in cases of Bence-Jones albumosuria would seem to point out the seat of production of this unusual proteid; but yet, when one considers the enormous quantities excreted daily—15 grammes in the above case—it is at first sight difficult to conceive how such a source can be possible. Magnus-Levy calculates that the whole mass of the diseased red marrow could not contain more than 100 grammes of proteid, and argues that, in his case<sup>1</sup> at least, where the daily excretion in the urine often attained 36 grms., its derivation from the bones was impossible. In support of this contention, he points out that in those cases where the total urinary nitrogen was estimated it was found that nearly 40 per cent. of this was excreted as Bence-Jones proteid. In a case investigated by Seegelken,<sup>2</sup> however, only about 10 per cent. of the total nitrogen was so excreted. From a consideration of these facts, Magnus-Levy supposes that the bone-marrow cannot be the seat of its production, but that it represents a non-assimilated digestive proteid. This want of assimilation he ascribes to the absence of some influence which the bone-marrow normally exercises on the metabolism of proteid, but which is wanting when the marrow is diseased.

In the above case, however, the results point to the bone-marrow as the seat of production, and the absence of any proteid in the

<sup>1</sup> Case No. 11 in the Summary.

<sup>2</sup> 'Deut. Arch. f. klin. Med.,' Bd. lviii, S. 276. (See Case No. 6 in the Summary.)

extract from nearly all the other tissues and organs would tend to disprove Magnus-Levy's theory, for were this correct we should expect to find at least some of the unusual proteid present in those organs (muscles, liver, etc.) where proteid metabolism is most active.<sup>1</sup>

The body was not found in the blood, and this was probably due to the fact that only a limited quantity was procurable for examination. Its presence in the kidneys was to be expected, since a certain amount of urine must still have been present in the tubules.

#### SUMMARY OF THE PRESENT CASE.

The patient, a rather fat man, aged 50, complained of rheumatoid symptoms, commencing, so he thought, about the end of the year 1899. About February, 1900, he began to suffer from pains in his loins and stiffness in the small joints of his hands. Soon afterwards the upper part of his back began to bend, so that he always had a stooping attitude. Previously to this illness the patient had been strong, but as a young man had had gonorrhœa and a chancre on the penis. One of his sisters suffered from diabetes mellitus.

The urine of the patient was found to contain the Bence-Jones proteid. The daily amount of the urine was about 2000 c.c., and it contained about 7 per mille of the proteid as measured by Esbach's albuminimeter. By a more exact method (precipitation with alcohol, drying and weighing) Dr. R. Hutchison found that about 15 grammes of the proteid were excreted daily. The reactions of the proteid were the typical ones described by Bence-Jones, Kühne, Bradshaw, etc.

For some time the patient's condition remained fairly stationary, and at first, by the use of local hot baths, massage, etc., the power of bending his fingers was

<sup>1</sup> It is certainly difficult to conceive how so much proteid could be derived from so small a source, but still, when we take into account other metabolic processes in the body, *e. g.* the occurrence of 30 grammes of urea in the urine and of only two grammes in the whole body, the result does not seem so surprising.

improved. Afterwards, however, the general weakness, cachexia, and anæmia greatly progressed, and gummatous disease of the tongue and over one rib made its appearance. Examination of the blood showed great anæmia and slight leucocytosis. On January 25th the patient died after copious hæmorrhage from the intestines, which post-mortem examination showed to be due to chronic ulceration of the duodenum. The Bence-Jones albumosuria persisted to the last.

At the necropsy the bone-marrow of all the bones examined was found to be more or less affected by a diffuse sarcoma-like growth of rounded or polyhedral mononuclear cells—a form of “multiple myeloma” or “myelomatosis.” There were no localised outgrowths projecting from the bones, such as have been noted in some cases of multiple myeloma, and no other parts of the body were invaded. In fact, as the neoplasm was strictly limited to the osseous system, no parts of it could be regarded as metastatic. The presence in the tumour-cells of certain granules and globules of various sizes constituted a striking histological feature in the present case.

Dr. R. Hutchison and Dr. J. J. R. Macleod made a careful chemical investigation of the bones, blood, and organs, but failed to find in any of these tissues and organs a body giving exactly the same reactions as those of the Bence-Jones proteid in the urine. From the vertebræ and ends of the femur, however, they obtained a proteid giving very similar reactions, differing somewhat in the temperature at which it coagulates and in not being re-dissolved on boiling. Moreover no proteid like that they detected could be derived, by employing the same methods, from normal red bone-marrow. They argue that in the present case the bone-marrow was probably the seat of production of the proteid excreted in the urine, and that this proteid is not a non-assimilated digestive proteid, as suggested by Magnus-Levy. Though the case was complicated with syphilitic gummata, chronic ulcera-

tion of the duodenum, and a generalised rheumatoid affection of the joints, it was a typical one of multiple myeloma with Bence-Jones proteid in the urine, the "myelopathic albumosuria" of Dr. T. R. Bradshaw, also called in Italy "Kahler's disease." When the diagnosis was first made it was probably the second case of the kind recognised during life in England, the first one being that of Dr. Bradshaw in 1898 (Case No. 10 in the Summary).

#### REMARKS ON MULTIPLE MYELOMA IN GENERAL.

Multiple myeloma may be defined as a diffuse new growth primarily involving the bone-marrow, especially that of the vertebræ, ribs, and sternum,<sup>1</sup> and affecting males as or more often than females, and chiefly those past middle age. The disease nearly always remains limited to the osseous system, though by direct extension it may form localised outgrowths projecting from the bones. Owing to absorption of the hard osseous tissue the bones become softened or friable; and are easily broken. The vertebral column and sternum are sometimes much bent, and the spinal cord may be affected by pressure, due to the curvature of the spinal column or to new growth bulging into the spinal canal. Owing to the destruction of bone-marrow the formation of blood is impaired, and anæmia and progressive cachexia occur, doubtless in some cases favoured by the circulation of a toxic proteid. I cannot help drawing an analogy between the bone disease, myelomatosis (*i. e.* multiple myeloma), on the one hand, and the skin disease, mycosis fungoides, on the other. In both cases the ætiology, as well as the

<sup>1</sup> In the present case, however, and in some other cases (see Nos. 20 and 24 in the Summary), the bones of the limbs were likewise much affected. Doubtless if the whole skeleton had been examined, the long bones would have been found affected in some of the cases in which by the clinical symptoms the bone disease was supposed to be limited to the ribs, sternum, and vertebral column.

true nature of the new growth, is obscure. For both diseases an infection theory has been propounded, making the new growths allied to the class of infective granulomata; but at present the arguments in favour of any such infection theory are far from convincing. In myelomatosis there is a primary diffuse infiltration of the bone-marrow of a great part of the skeleton, followed in some cases by the formation of definite localised tumours growing from the bones; whilst mycosis fungoides usually commences as a diffuse infiltration of the skin (præmycotic stage), and the localised tumours, which give the disease its name, begin to sprout out later on. This analogy may perhaps turn out to be a very superficial one, but in the present uncertainty regarding both diseases it is worthy of mention. In one important point, indeed, the analogy is imperfect. The point is that, whilst mycosis fungoides seems to be a single definite disease (morbid entity), different kinds of neoplasm have apparently been included under the heading "multiple myeloma."

Multiple myeloma is a term which has been employed to include various diffuse new growths arising in the bone-marrow (*i. e.* myelogenic), and not giving rise to definitely metastatic growths in other tissues.<sup>1</sup> After post-mortem investigations various names have been employed according to the histological features (and individual interpretations by observers) of the neoplasms, and particularly of the cell-elements of which the tumours are formed. The tumours have been regarded as simple overgrowth of the cell-elements of the bone-marrow, or as myelogenic sarcoma, endothelioma, perithelioma, plasmoma, etc. In my first case<sup>2</sup> of "multiple myeloma" I supposed the tumour formation to be an example of "general lymphadenomatosis of bones." I have lately been able to re-examine the growth and get sections

<sup>1</sup> See later on in regard to the lymphatic glands becoming affected in some cases.

<sup>2</sup> "General Lymphadenomatosis of Bones, one form of 'Multiple Myeloma,'" 'Trans. Path. Soc.,' 1897, *loc. cit.*



stained by special methods. Following is a short abstract of the case :

The patient, E. P—, a man aged 61 years, was admitted to the German Hospital October 17th, 1896, complaining of various pains, resembling those often described in rheumatoid arthritis. His illness was apparently of comparatively recent onset. He was rather emaciated, and looked older than he really was—more like a man of 80 than of 61 years. He walked very stiffly and carefully with the aid of a stick. There was considerable kyphosis, and this seemed to be progressive. No organic disease could be found in the viscera, and the urine, according to the single note entered, was free from albumen. The blood was unfortunately not examined. Various medicines were tried, including glycerophosphates, iodide of iron, and arsenic, but they had no obvious effect. The patient had a fair appetite, and was free from fever; yet he seemed to get weaker and to complain more of the pains. The bilateral pains in the sides of the abdomen, which were usually worse when the patient stood up, and the increasing lumbo-dorsal kyphosis made one think of the possibility of malignant disease of the spinal column, of vertebral caries, or of spondylitis deformans. The whole spinal column was kept rigidly fixed in one position. In December pneumonia developed and led to the patient's death on January 18th, 1897.

The *necropsy* showed greyish consolidation of the bases of both lungs. The heart presented nothing unnatural. The stomach was abnormally dilated. The spleen was slightly enlarged and soft, and its capsule was thickened. The liver, by macroscopical and microscopic examination, appeared normal. The kidneys had undergone a moderate degree of interstitial fibrosis, and in the cortex of one of them calcareous granules (microscopic calculi) were present, some of which were in close relation to minute cystic adenomata.

All the ribs, the whole vertebral column, the clavicles, the sternum, and the bones of the calvarium were examined, and were all found to be the site of a very vascular pulpy neoplasm, growing from the interior outwards. The ribs were converted into delicate tubes formed of periosteum, with only a thin, imperfect shell of bone; they were all stuffed full of the new growth. The slightest pressure sufficed to break them in any part. Many "spontaneous" fractures had occurred during life, and had already been thoroughly united by callus. Here and there the osseous tissue had been completely absorbed, so that the new growth lay directly under the periosteum, and in some places the periosteum and bony shell had been bulged out by the tumour so as to form nodular enlargements on the

ribs. The clavicles were somewhat less affected than the ribs, sternum, and vertebral column. There was a certain amount of new growth in the diploë of the cranial bones. Specimens of the new growth from the vertebræ, ribs, and diploë of the skull were microscopically examined, and consisted of rather small mononuclear cells, with none, or scarcely any substance between them. Interspersed amongst the cells were small blood-vessels, with swollen-looking, almost hyaline walls.<sup>1</sup> Examination of spicules of bone taken from the growth seemed to show that the bone was being absorbed by the tumour formation without undergoing any preliminary process of softening (decalcification), such as is reported to occur in osteomalacia and in the absorption of the bone trabeculæ in the long bones in some cases of pernicious anæmia.<sup>2</sup>

I have not yet mentioned that behind the right clavicle some enlarged lymphatic glands were found, which the microscope showed to be the site of a similar (but less vascular) growth to that of the bone-marrow. No tumour was discovered in other lymphatic glands or elsewhere in the body.

Recent re-examination of old sections (stained by the ordinary methods) from the bone-marrow growth, and from the affected glands, has confirmed the view and made it practically certain that the growth in the glands is identical with that in the bones. The cells of which the growth consists resemble lymphocytes, except that very many of them have more protoplasm than ordinary small lymphocytes have. The larger cells are rounded, oval, or polyhedral, and the nucleus is often placed excentrically. Part of the sternum was fortunately preserved in glycerine and formalin in the Museum of the Royal College of Surgeons, and thus I have lately had an opportunity of examining sections of the sternal portion of the growth stained by Ehrlich's tri-acid and by Mann's eosin-methyl-blue combinations. These stains show that hardly any of the cells contain granules. In fact, only one or two coarsely granular eosinophile cells were seen in looking through the sections, and these were probably not tumour-cells. The tumour may, therefore, be said to consist of non-granular, lymphocyte-like cells. The majority of these cells have more protoplasm than ordinary small lymphocytes have. It must be remembered, however, that in lymphatic leucocythæmia the growths in the various organs may

<sup>1</sup> From recent examination of portions of the growth from the sternum, I think that some of these supposed vessels are really vesicles remaining from fat-cells.

<sup>2</sup> Cf. "On the Changes of the Bone-marrow in Pernicious Anæmia," by R. Muir, 'Journal of Pathology,' 1894, vol. ii, p. 363.

consist largely of cells which, though they are described as lymphocyte-like, have much more protoplasm than do the small lymphocytes of normal blood. Every intermediate form between the cells with much protoplasm and those with very little protoplasm can be found in the growths of lymphatic leucocythæmia; and so they can be in the myelogenic growth from the patient E. P—. Moreover in normal lymphatic glandular tissue many of the cells of the "germinating centres" have more protoplasm than the small lymphocytes further from these centres and in the circulating blood. I feel justified, therefore, in saying that in the case of E. P— the cells of the myelogenic growth were lymphocyte-like, if not actually of the lymphocyte kind. Dr. J. M. H. MacLeod has kindly examined the growth by special staining for plasma-cells, and thinks that the cells of which the growth is composed have a greater resemblance to lymphocytes than to the typical plasma-cells of the granulomata.<sup>1</sup>

Two types, if not more, of "multiple myeloma" are to be distinguished—(1) a growth, as in the patient J. T—, in which the bone-marrow only is involved; (2) a growth in which nearly all the cells resemble small or large lymphocytes, and are possibly derived from the non-granular predecessors of the myelocytes;<sup>2</sup> in this second type of "multiple myeloma" lymphatic glands as well as bone-marrow may probably be affected. The second type of multiple myeloma would include cases described as myelogenic lympho-sarcoma, myelogenic lymphadenoma, and myelogenic pseudo-leukæmia (using the German term "leukæmia" in the limited sense of "lympho-cythæmia"). Intermediate cases between these two types ("mixed forms") probably also occur (cf. remarks under Case No. 16 in the Summary at the end).

<sup>1</sup> I may add that in part of the growth in the sternum many of the tumour-cells have undergone some kind of a degenerative change, owing to which, by Mann's eosin-methyl-blue combination, the nucleus and the rest of the cell are deeply stained by the eosin.

<sup>2</sup> Cf. A. Pappenheim, 'Virchow's Archiv,' 1902, vol. clxix, p. 381. According to his views the *large lymphocyte* type of cell, which in the lymphatic glands gives rise to the ordinary small lymphocytes of the blood, in the bone-marrow gives rise to the myelocytes and thus indirectly to the polymorphonuclear leucocytes also.

If the views which I have suggested in this paper be correct, it follows that the *whole class of leukæmias and pseudo-leukæmias* (using the German terms for convenience) can be divided into at least the following six types, independently of intermediate forms:

(a) A new growth of lymphocyte-like cells originating in the bone-marrow and not overflowing into the circulating blood.—Myelogenic pseudo-leukæmia (using leukæmia in the sense of lympho-cythæmia), myelogenic lympho-sarcoma, lymphadenomatosis of bones, multiple myeloma (myelomatosis) of the lymphatic type.

(b) Similar to the preceding, but the lymphocyte-like cells overflow into the blood-stream.—Myelogenic lympho-cythæmia. I do not know of any cases illustrating this type, excepting cases of "acute leukæmia." Those of A. Dennig<sup>1</sup> and C. H. Melland,<sup>2</sup> for instance, were examples of acute lympho-cythæmia in which post mortem practically no change was discovered in the leucocyte-forming tissues other than the bone-marrow.

(c) A new growth formed in large part of lymphocyte-like cells originating in the lymph-glands or lymphadenoid tissues generally, and not to any great extent overflowing into the circulating blood.—Lymphatic or splenic lymphadenoma or pseudo-leukæmia (using leukæmia in the sense of lympho-cythæmia), Hodgkin's disease. In the more chronic and fibrous varieties of this type the microscopic appearances differ, of course, considerably from those in acute cases.

(d) Similar to the preceding, but the lymphocyte-like cells invade the blood-stream.—Lymphatic or splenic lympho-cythæmia.

(e) A new growth, originating in the bone-marrow, of cells derived from the myelocytes, not invading the circulating blood.—Myelogenic pseudo-leukæmia (using leukæmia in the sense of myelogenic or spleno-medullary

<sup>1</sup> 'Muenchener medicinische Wochenschrift,' January 22nd, 1901, No. 4, p. 140.

<sup>2</sup> 'Medical Chronicle,' September, 1902, p. 372.

leucocythæmia). To cases of this type the term *multiple myeloma* (*myelomatosis*) might perhaps be limited.

(f) A new growth characterised by its myelocyte-like cells overflowing or being drawn out into the circulating blood, and by Bence-Jones albumosuria not occurring, as it sometimes does in the last type (e).—Myelogenic or spleno-medullary leukæmia (leucocythæmia).

According to this scheme one must regard the excess of white corpuscles in the blood in all kinds of leukæmia as due to an inroad of tumour-cells from a *hyperplasia-like* tumour-formation in the leucocyte-forming tissues of the body,<sup>1</sup> all forms of leucocytosis (including lymphocytosis) being merely expressions of some reaction in the tissues in question. A leucocytosis is therefore, strictly speaking, never an early stage of leukæmia (leucocythæmia); yet a true leucocytosis from any cause may perhaps sometimes be followed by true leukæmia, in so far as a reactive growth in leucocyte-forming tissues (of which, reactive growth the leucocytosis is the expression) may be supposed to give a start to the kind of tumour-formation of which the leukæmia is the expression, just as chronic irritation of the skin sometimes acts as the exciting cause of epithelioma.

#### REMARKS ON MULTIPLE MYELOMA WITH BENCE-JONES PROTEID IN THE URINE.

I shall now, however, confine my remarks to the present case and similar cases in which multiple myeloma is associated with the presence of Bence-Jones proteid in the urine. Though their microscopic appearances may somewhat vary, the growths in this group of cases are allied to each other by one notable peculiarity—a metabolic one—namely, that they form or cause to be formed in the body a substance which is got rid of by the kidneys as Bence-Jones proteid. Some striking features in the present case deserve special consideration.

<sup>1</sup> Cf. Pappenheim's various writings, loc. cit., etc.

## SPECIAL FEATURES OF THE PRESENT CASE.

*The articular disease.*—It was the affection of the hands, amounting to a "pseudo-paralysis," that obliged the patient to give up work and seek the hospital. The history in this respect is important. He was a stout, middle-aged, sallow-looking man, suffering from tingling sensations in the tips of his fingers (a kind of "acro-paræsthesia") and inability to grasp objects. He could not close his hands, and any attempt to bend his fingers caused pain. The back of the hands had a puffy, swollen appearance, especially about the metacarpo-phalangeal joints, and the fingers were tremulous. There was some pigmentation of the skin, and the fleshy portions of the finger-tips were shrivelled. The shoulder-joints were also somewhat affected, and doubtless the wasting noticed in the muscles of the upper extremities could be accounted for by the articular affection. After death from other causes marked changes were found in the joints examined—namely, in the hip, shoulder, wrist, and fingers. There can be no doubt that the patient suffered from a form of rheumatoid or rheumatic<sup>1</sup> arthritis, and that most of the early symptoms which he complained of were due to the arthritic affection, not to the myelomatosis of bones.

Whether or not the tumour-formation in the bones had any causal connection with the articular disease must remain doubtful. That joint changes can be induced by the irritation set up by tumour-formation in the neighbouring bones is made probable by an observation of Mr. Jonathan Hutchinson.<sup>2</sup> His case was that of a young woman whose thigh was amputated for a tumour of the tibia, and in whose knee-joint changes were discovered such as occur in rheumatoid arthritis.

The articular symptoms in the present case may be

<sup>1</sup> The evidence of former endocarditis found in the heart suggests that at one time there was acute rheumatism.

<sup>2</sup> 'Mod. Times and Gazette,' 1881; quoted in Fagge and Pye-Smith's 'Principles and Practice of Medicine,' vol. ii.

compared to those of a type of early rheumatoid arthritis, referred to by Dr. J. Kent Spender,<sup>1</sup> in which the commencement is by sudden weakness in the hands. The patient complains that the hands cannot "hold" and that the fingers are "going to be paralysed," and there may be paræsthesia described as "burning," "scalding," or "scraping," together with vaso-motor disturbance. In the present instance the "pseudo-paralysis" of the hands, though it was to some extent relieved by local treatment (hot baths, massage, etc.), was explained by the structural changes (synovial fringes, etc.) in the small joints, which were still present when the patient died from other causes. The articular affection was, however, certainly not limited to the hands, as the post-mortem examination showed, though it was the inability to use his fingers that roused the patient's attention and obliged him to give up work.

I should like in passing to draw attention to a characteristic feature in certain affections of the small joints of the upper extremities, to which I believe sufficient attention has not yet been paid—namely, the presence of tremor of the fingers. This tremulousness<sup>2</sup> of the fingers is very characteristic when associated with a puffy swelling of the back of the hand, with a certain amount of shrivelling of the finger-tips, with inability to flex the phalangeal and metacarpo-phalangeal joints, and consequently with loss of power to grasp objects. The tremors are best observed when the fingers are separated or when the patient is endeavouring to move either his fingers or his whole hand. Each finger trembles as a whole from the metacarpo-phalangeal articulation, and the movements constituting the tremor in each finger are not necessarily synchronous with those in the other fingers. The type is therefore rather that of alcoholic and of certain other toxic tremors.

<sup>1</sup> Allbutt's 'System of Medicine,' vol. iii, p. 81.

<sup>2</sup> Perhaps the word "tremulousness" suits the irregularity of the movements better than "tremor" does; but the latter is shorter, and is, I believe, generally used to include all movements which are quick, small, and frequent, even if not strictly rhythmical in character.

This tremor may be unilateral in cases of gonorrhoeal rheumatism of the wrist and hand, in which disease it is apt to occur during the subacute or chronic stage associated with trophic changes in the fingers and muscular wasting,—that is, at a period when the disease often resembles chronic tuberculosis of the wrist-joint. In connection with the tremor the negative result from examination of the nervous system in the present case is perhaps worthy of remark, though it is what one would expect.

*The syphilitic affection.*—The gummatous disease of the tongue and rib makes it clear that the patient really had syphilis, although he could not remember having had a secondary eruption. Considering how apt tertiary syphilis is to affect the bones, it is just possible that in this case it may have acted as an exciting cause in regard to the tumour-formation (myelomatosis).<sup>1</sup> In a similar way the irritation of the osseous changes in osteitis deformans and chronic osteomalacia<sup>2</sup> may be supposed sometimes to excite the development of primary bone-

<sup>1</sup> It is worth mentioning that in the case described by Sir H. Weber in 1866 ('Trans. Path. Soc.,' 1867, vol. xviii, p. 206), which would probably now be regarded as one of multiple myeloma, the patient, a man forty years of age, had had syphilis fourteen to sixteen years before death, and had amyloid disease of the kidneys and spleen. The sternum, ribs, vertebral column, and cranium were affected by a growth which Hulke and Cayley, who reported on it, were inclined to regard as sarcomatous. The state of the urine is not alluded to. The alteration in shape of the sternum was so great that it caused pressure on the aorta with physical signs simulating aneurysm.

<sup>2</sup> The occasional occurrence of primary malignant tumours in the bones in cases of osteitis deformans has been recognised since Sir James Paget's original description of the disease in 1876 ('Med.-Chir. Trans.,' vol. lx). Dr. Wilhelm Schötenberger ('Virchow's Archiv,' 1901, vol. clxv, pp. 189—226) gives the case of a woman aged 33 in which the changes of osteomalacia apparently preceded the development of multiple sarcomata (multiple fractures had also occurred). He likewise speaks of solitary or multiple sarcomata often developing in the late stages of "osteomalacia chronica deformans hypertrophica." It may be asked, however, whether these late forms of osteomalacia (showing a kind of hypertrophic reaction with new bone-formation) are not identical with osteitis deformans except for their history.



tumours, and chronic malaria seems occasionally to have acted as an exciting cause in the development of leucocythæmia.<sup>1</sup> On the whole, however, it is more probable in the present case that the cachectic condition of the patient led to the outbreak of tertiary syphilis. For, in syphilitic subjects, fevers and other general debilitating conditions, and (locally) traumatisms, favour the onset of gummatous disease.

*The duodenal ulceration.*—There is no doubt that the severe intestinal hæmorrhage greatly accelerated death in the present case. This may partly account for the fact that in the patient in question the tumour had, at the time of death, caused less destruction of bony tissue than in certain other patients with multiple myeloma; but it must also be noted that the man was strongly built, and the outside of his bones may have been specially resistant. Most patients with multiple myeloma, as I pointed out in 1897,<sup>2</sup> die of pneumonia, but the fatal result of the hæmorrhage in the present case interfered with the ordinary course of events. The duodenal affection is probably to be classed with the duodenal ulcers associated with renal disease.<sup>3</sup> The excretion of an irritant substance by the intestinal mucous membrane possibly accounts not only for duodenal ulceration, but also for ulcerative colitis when occurring in cases of renal disease.

#### THE BENGE-JONES PROTEID IN THE URINE OF MULTIPLE MYELOMA CASES.

The reactions of the proteid in the urine have already been described in the report by Drs. Hutchison and Macleod. They conclude that in the present case the

<sup>1</sup> For instance, in the case of leucocythæmia with Menière's symptoms which I communicated in 1900 ('Med.-Chir. Trans.,' vol. lxxxiii, p. 185).

<sup>2</sup> 'Trans. Path. Soc.,' vol. xlviii, loc. cit.

<sup>3</sup> See "On Diseases of the Duodenum," by E. C. Perry and L. E. Shaw, 'Guy's Hospital Reports,' 1893, vol. 1, pp. 194—196 and 250—255.

bone-marrow was probably the seat of production of the proteid in question, and that this proteid is not a non-assimilated digestive proteid, as suggested by Magnus-Levy.<sup>1</sup> As confirming their views, I will repeat that in my patient a considerable alteration of diet maintained during two days had no effect in altering the quantity of proteid excreted in the urine. Moreover Dr. Bradshaw, in his case, found that meals had little or no influence on the excretion of the proteid in the urine. He found that as much was excreted by night as by day,<sup>2</sup> when the patient was taking meals during the daytime only; and he considered the rate of excretion to be "pretty constant throughout the twenty-four hours."

• It seems probable that when it is free in the blood the Bence-Jones proteid appears in the urine,<sup>3</sup> like hæmoglobin does whenever owing to various causes sudden unusual hæmolysis occurs. The fact, therefore, that the quantity excreted in the urine is little influenced by meals and by change of diet speaks strongly against the correctness of Magnus-Levy's views. It is possible that the cells of the new growth in the bone may produce digestive enzymes, by the action of which on the albuminous constituents of the blood-serum the Bence-Jones proteid is steadily and continually manufactured. Then from the circulating blood it would pass through the renal filter with the urine, like hæmoglobin, even in the absence of any kidney disease. As already mentioned, there may be some connection between the excretion of the proteid in the urine and the formation of granules and globules in the cells of the new growth in the present case.

<sup>1</sup> Loc. cit.

<sup>2</sup> See the tables at the end of Dr. Bradshaw's first paper ('Med.-Chir. Trans.,' 1898, vol. lxxxi, pp. 270, 271).

<sup>3</sup> Stokvis found that Bence-Jones proteid, when a not very concentrated solution was injected into the rectum of a dog, was excreted unchanged in the urine. I have to thank Sir Lauder Brunton for directing my attention to these little-known experiments of Stokvis, which were recorded in the 'Maandblad der sectie voor Natuurwetenschappen,' 1872, No. 6.

DIAGNOSIS OF MULTIPLE MYELOMA (MYELOMATOSIS) WITH  
AND WITHOUT BENCE-JONES PROTEID IN THE URINE.

There is still much uncertainty as to the nature of multiple myeloma (Multiples Myelom), a term first employed by J. von Rustizky,<sup>1</sup> who regarded the growth as formed by a simple hypertrophy of bone-marrow. As already mentioned, however, the tumours from different cases do not all resemble each other in their histological features, though they possess certain characters in common. The growth is generally so diffuse in its distribution that it is impossible to determine that any one part represents a primary focus where the neoplasm may be supposed to have commenced. It does not invade other tissues by metastasis through the blood-channels like sarcoma does, though in some cases the lymphatic glands have been involved (cf. Case 3 in the Summary at the end).

Owing to the softening and fragility of bones, the pains, and the progressive kyphosis caused by the disease, the diagnosis is firstly from—

- (a) *Osteomalacia.*
- (b) *Muscular rheumatism, lumbago, sciatica, etc.*
- (c) *Spondylitis deformans.*
- (d) *Caries of the spinal column.*
- (e) *Invasion of the vertebral column and other bones by secondary malignant tumours.*

Owing to the progressive anæmia and cachexia, one may think of—

- (f) *Pernicious anæmia or other diseases associated with progressive cachexia.*

Owing to the possibility of confusing Bence-Jones proteid in the urine with albumen, the cases of multiple myeloma in which this body is present in the urine (*i. e.*

<sup>1</sup> "Multiples Myelom," 'Deutsche Zeitschrift für Chirurgie,' Leipzig, 1873, vol. iii, p. 162.

the cases of "myelopathic albumosuria" of Bradshaw, "Kahler's disease") may be at first mistaken for—

(g) *Nephritis*.

(a) *Osteomalacia*.—From the typical osteomalacia of women multiple myeloma differs in the following respects. The former attacks women during the child-bearing period of life. It affects chiefly the bones of the pelvis and lower extremities. It gives rise to great deformity by the bending of the bones, but more rarely to "spontaneous" fractures. Multiple myeloma attacks men as often as women, or more often, and chiefly those in the second half of life. Clinically, it appears specially to affect the vertebral column, ribs, and sternum, though the bones of the extremities have certainly been involved in some cases, as they were in my present case. It is likely to cause fractures of the ribs and deformity by bending of the vertebral column and sternum; in one case (Case No. 20 in the Summary) "spontaneous" fracture of one femur occurred, and in another (Case No. 24 in the Summary) "spontaneous" fractures of both femora are recorded; yet it does not give rise to the characteristic deformities of osteomalacia, resulting from yielding of the pelvis and bending of the bones of the lower extremities. It is possible, however, that there may be true cases of osteomalacia in males and in elder females, in which the bones of the vertebral column and trunk are specially affected.

(b) *Muscular rheumatism, lumbago, sciatica, etc.*—Several cases of multiple myeloma have, at least during part of the disease, been given such headings. The occurrence of markedly bilateral thoracic, abdominal, or lumbago-like pains may first direct attention to the possibility of disease of the spinal column. In my first case of multiple myeloma,<sup>1</sup> pain on both sides of the abdomen, together with the presence of an increasing kyphosis, pointed to grave disease of the spinal vertebræ. Some-

<sup>1</sup> 'Trans. Path. Soc.,' loc. cit.

times examination of the bones by Röntgen's rays may prove of service (*vide* Case No. 13 in the Summary at the end). If grave rheumatoid or rheumatic arthritis is a complication, as in my present case, it obviously becomes difficult to distinguish pains and paræsthesiæ due to the arthritis from those due to the multiple myeloma.

(c) *Spondylitis deformans*.—This affection of the vertebral columns may produce a similar kyphosis to that which in several cases has been caused by multiple myeloma. When, however, the kyphosis is due to spondylitis deformans,<sup>1</sup> the spinal rigidity in the cervical region is probably more pronounced than in cases of multiple myeloma, whilst the patient is likely to be less anæmic and cachectic. For comparison with my illustration of the present case of multiple myeloma (Plate I), I am able, by the kindness of my colleague, Dr. zum Busch, to give the illustration of a spondylitis deformans patient (the so-called "spondylose rhizomélique" type of Pierre Marie, at a relatively early stage of the disease) (Plate II) under his care, whom I also had formerly seen in the out-patient department. The portrait of Dr. Bradshaw's patient, illustrating his paper before the Medical and Chirurgical Society of London in April, 1898 ('Transactions,' 1898, vol. lxxxi, Plate VII), should likewise be consulted for comparison (reproduced here by permission, Plate III).

(d) *Curves of the spinal column*.—The progressive bend-

<sup>1</sup> Cases in which the vertebral column only is affected (von Bechterew's type) may be distinguished from those in which the extremities, especially the hip-joints, are likewise affected (Strümpell's type, Pierre Marie's "spondylose rhizomélique"). Such cases of chronic ossifying arthritis may progress to universal bony ankylosis. (See the summary of cases by Dr. Joseph Griffiths in the 'Journal of Pathology and Bacteriology,' December, 1896, and March and June, 1897. Much has been written on the subject during recent years in France and Germany.) Of course, when ankylosis of the joints of the extremities has occurred, a case could hardly be mistaken for one of multiple myeloma, but even at the commencement of the disease such a mistake is very unlikely to be made.

ing of the vertebral column seen in multiple myeloma might be confused with tuberculous caries,—that is, with those rather rare cases occurring in middle or old age and giving rise to progressive curvature. On the other hand, the curvature due to myeloma is somewhat less likely to be distinctly “angular” than that due to tuberculosis, and in the latter disease the ribs are not likely to be in any way affected simultaneously with the spinal column. The sternum has sometimes become excessively bent in multiple myeloma. The presence of tuberculosis in the lungs might help to clear up the diagnosis.

(e) *Invasion of the vertebral column and other bones by secondary malignant tumours.*—Secondary localised malignant tumours may give rise to a progressive curvature of the vertebral column. The vertebral column and ribs may likewise be diffusely infiltrated by metastatic carcinoma, but all such metastatic growths are more likely to cause distinct swellings<sup>1</sup> or give rise to local signs of their presence. Evidence as to a primary malignant growth existing or having been removed from some other part of the body would facilitate the diagnosis, and in localised tumours, as well as in tuberculous caries, help might be obtainable from the Röntgen rays.

(f) *Pernicious anæmia, etc.*—Anæmia and progressive wasting and feebleness may be marked features of myelomatosis, at all events in the later stages, when the blood-forming functions of the bone-marrow are greatly impaired by the diffuse tumour-formation. The pains and other signs of bone disease, such as progressive kyphosis, when these are well marked, will help to distinguish cases of multiple myeloma from pernicious anæmia and forms of progressive cachexia dependent on visceral cancer, etc.

(g) *Nephritis.*—The Bence-Jones proteid when present in the urine may be confused with albumen, and the case

<sup>1</sup> In some cases, however, of multiple myeloma, with or without Bence-Jones proteid in the urine, localised tumours connected with the bones could be seen or felt during life. (See Cases 14, 19, 27, and 33 in the Summary at the end.)

may be regarded as one of nephritis. This is especially likely to occur if the urine on the first occasion is examined very hurriedly (for example, by heating it without boiling it, or by merely adding picric acid or nitric acid in the cold), and, owing to the copious precipitate of supposed ordinary albumen, it is subsequently examined every day by Esbach's tube. This actually occurred in the present case,<sup>1</sup> where the general "puffy" look of the patient seemed to correspond to the finding of albuminuria. Moreover in this case, as in some other cases, hyaline casts were found in the urine.<sup>2</sup> Afterwards the testing of the urine by the ordinary methods, instead of by Esbach's solution, led to the detection of the special proteid it contained.

I need not repeat what has already been said in regard to the tests to be employed for distinguishing Bence-Jones proteid in the urine from albumen and from certain albumoses.<sup>3</sup> In the albumosuria occasionally met with in cases of intestinal ulceration and febrile disorders, the quantity of proteid in the urine is generally far less than in Bence-Jones albumosuria. In such a case as that recorded by Dr. R. Hutchison,<sup>4</sup> where the proteid, though precipitated at as low a temperature as 58° C., was not, even partially, re-dissolved on heating to the boiling-point, the chances of wrongly regarding the precipitate as

<sup>1</sup> The remarkable constancy in the amount and the large quantity of the proteid in the urine ought perhaps to have caused some surprise.

<sup>2</sup> The necropsy, it should be remembered, showed the presence of actual interstitial fibrotic changes in the kidneys. In Senator's case (Case No. 7 in the Summary) casts and albumen were present in the urine, and the kidneys were found to be somewhat diseased at the post-mortem examination. In d'Allocco's case (No. 15) there was likewise nephritis; in Ellinger's (No. 9) the urine contained a few hyaline casts; and in Conti's (No. 27) during the last weeks of life the urine contained albumen and hyaline and granular casts.

<sup>3</sup> I do not think that Dr. L. N. Boston's caustic soda and lead acetate test ("A Rapid Reaction for Bence-Jones Albumose," 'American Journ. Med. Sci.,' October, 1902, p. 567) is likely to be of much service in this connection.

<sup>4</sup> Case No. 30 in the Summary of cases at the end.

one of ordinary urinary albumen must be still greater than they were in the present case, where the greater part of the precipitate re-dissolved on boiling the urine.

I now come to the *diagnostic value of finding Bence-Jones proteid in the urine*. From a study of cases the following conclusions must be arrived at:—(1) Undoubtedly a considerable number of cases of multiple myeloma have occurred in which the Bence-Jones proteid has not been detected. In some of them the urine may have been examined at a stage of the disease prior to the commencement of the "Bence-Jones albumosuria."<sup>1</sup> In other cases the urine may possibly have been insufficiently examined. Still there remain sufficient cases to enable one to affirm with almost absolute certainty that "multiple myeloma" may occur without giving rise to the presence of Bence-Jones proteid in the urine. It must be remembered, however, that different types of tumour have been included under the heading "multiple myeloma," but I will not repeat here the conclusions which I have already mentioned in an earlier part of the present paper. (2) Metastatic tumours affecting the skeleton, however extensively the bone-marrow be infiltrated, have never yet been known to cause "Bence-Jones albumosuria." (3) The presence of Bence-Jones proteid in the urine is almost invariably of fatal significance, and nearly always, if not always, indicates that the patient is suffering from "multiple myeloma." (4) One or two published cases in which Bence-Jones proteid was present in the urine seem, however, to have been exceptions to the rule, in that they were supposed not to be instances of multiple myeloma. Moreover the experiments of Dr. G. Zuelzer,<sup>2</sup> should they be confirmed,

<sup>1</sup> In the case of Stokvis and Kühne (Case No. 2 in the Summary), the Bence-Jones proteid is said to have appeared late in the disease, and could not be found three months before the patient's death. Conti says that during the last weeks of life in his case (No. 27 in the Summary) the urine contained albumen but no Bence-Jones proteid.

<sup>2</sup> "Ueber experimentelle Bence-Jones'sche Albumosurie," 'Berliner klinische Wochenschrift,' 1900, No. 40, p. 894.



would make the existence of such exceptions more probable. He rendered a dog anæmic by giving it pyrocin by the mouth. On the eighth day from the commencement of the experiment, a substance was detected in the urine giving the typical reactions for Bence-Jones proteid, and no albumen was present. The pure Bence-Jones albumosuria lasted four days, and then albuminuria occurred and the amount of the Bence-Jones proteid diminished. It would be interesting to know what changes occurred in the bone-marrow of this animal.

Taking all the data that I can obtain into consideration, it seems to me quite possible (1) that Bence-Jones albumosuria is always the result of disease of the bone-marrow; (2) that it is due to an abnormal metabolic or degenerative process in the myelocytes or in tumour-cells derived from the myelocytes or their predecessors; (3) that the reason why it is generally, though not always,<sup>1</sup> associated with myelogenic tumour formation is that the tumour-cells derived from bone-marrow cells, however much they may morphologically resemble true bone-marrow cells, are more prone to abnormality (including unusual degenerative changes) than real myelocytes are; (4) that non-myelogenic tumour-cells are not affected in the same way, and therefore metastatic tumours in the bone-marrow do not give rise to Bence-Jones albumosuria.

In further evidence of the correctness of these conclusions, I shall now give a very short summary of all the reported cases in which Bence-Jones proteid has been detected in the urine,<sup>2</sup> whether the presence of bone

<sup>1</sup> An analogy between Bence-Jones albumosuria and melanuria may be made. The presence of melanin and melanogen in the urine is best known in cases of melanotic tumour, but has been noted likewise in wasting diseases. Melanotic tumours, however, are not always associated with the excretion of melanin or melanogen in the urine. Yet, as Dr. A. E. Garrod points out ('St. Bart.'s Hosp. Rep.,' vol. xxxviii, p. 25), melanuria has been undervalued for diagnostic purposes because other conditions in which the urine blackens on exposure to air have been confounded with true melanuria.

<sup>2</sup> In preparing the list I am indebted to the summaries given in

disease was verified or not. I shall also refer to some doubtful cases, in which the reactions of the proteid in the urine were not quite characteristic for Bence-Jones proteid, and shall mention certain supposed cases obviously incorrectly included in previous summaries on the subject. For full details, however, the original papers, to which references are given under each case, must be consulted. Amongst doubtful cases are those, such as that reported by R. Hutchison (Case No. 30), in which, though a copious precipitate occurs on slightly heating the urine, yet this precipitate is not to any extent dissolved by further heating. In this connection it must be remembered that the experiments of Hammarsten,<sup>1</sup> K. Spiro,<sup>2</sup> Magnus-Levy,<sup>3</sup> and others in regard to various proteids, show that the point of heat coagulation varies with the dilution and composition of the fluid, and the resolution of the coagulum depends likewise to a great extent on the composition of the fluid in which it is suspended. Amongst cases which should not be included in the Summary are those of albumosuria (other than "Bence-Jones albumosuria") in which no precipitate occurs on merely heating

various previous articles on the subject, particularly to that of Dr. C. E. Simon (*vide* Case No. 20). I shall not here refer to the cases of "multiple myeloma without albumosuria," several of which are quoted in my paper in vol. xlviii of the 'Transactions of the Pathological Society of London' (*loc. cit.*). On the whole subject of multiple myeloma, the important writings of F. W. Zahn ('*Deut. Zeitschr. f. Chirurgie*,' 1885, vol. xxii, p. 1), Hammer ('*Virchow's Arch.*,' vol. cxxxvii, p. 280), Markwald ('*Virchow's Arch.*,' vol. cxli, p. 128), R. Paltauf ('*Ergebnisse der allg. Pathologie*,' edited by Lubarsch and Ostertag, 1896, vol. i, pp. 676—679), K. Winkler ('*Virchow's Arch.*,' vol. clxi, p. 252), E. Wieland ('*Virchow's Arch.*,' vol. clxvi, p. 103), and M. Borst ('*Die Lehre von den Geschwülsten*,' 1902, vol. i, pp. 492—494) may be consulted. I have not studied the long paper by Dr. F. Harbitz on multiple primary tumours of bones (in the '*Norsk Magazin for Lægevidenskaben*,' Christiania, 1903, Nos. 1 and 2), but in none of Harbitz's cases was Bence-Jones proteid detected in the urine.

<sup>1</sup> *Loc. cit.*

<sup>2</sup> *Loc. cit.*

<sup>3</sup> *Loc. cit.*

the urine (presumably acid in reaction), but in which the addition of nitric acid to the cold urine gives rise to a precipitate, which dissolves on heating and reappears on cooling.<sup>1</sup>

#### SUMMARY OF CASES.

No. 1. *The case of Watson, Macintyre, and Bence-Jones, of London.*—(H. Bence-Jones, "On a New Substance occurring in the Urine of a Patient with Mollities Ossium," 'Phil. Trans. Royal Society, London,' London, 1848, Part i, p. 55. W. Macintyre, "Case of Mollities and Fragilitas Ossium," 'Med.-Chir. Trans.,' London, 1850, vol. xxxiii, p. 211. J. Dalrymple, "On the Microscopical Character of Mollities Ossium," 'Dublin Quarterly Journ. Med. Sci.,' 1846, vol. ii, p. 85.)

The patient was a man aged 45, a patient of Dr. W. Macintyre and Sir Thomas Watson. His pains commenced after a strain in September, 1844. The proteid was present in the urine when a specimen was sent to Bence-Jones in November, 1845. Death occurred in

<sup>1</sup> A typical example of this is recorded by Hougoumenq ('Lyon Médical,' vol. xcvi, Jan. 20th, 1901). See also E. Vidal's case ('Comptes rendus de la Société de Biologie,' October 29th, 1898, p. 991) in a woman, aged 24, suffering from tuberculous disease of the right shoulder. Dr. J. A. Blair's "Case of Albumosuria" ('Brit. Med. Journal,' September 14th, 1901, p. 713) is doubtless of the same kind. He states that the urine "gave no perceptible precipitate on simple heating without acid," but that on adding nitric acid to the cold urine a precipitate occurred which was dissolved on heating and reappeared on cooling. This kind of albumosuria is doubtless much less rare than the "Bence-Jones albumosuria," and is probably sometimes altogether overlooked owing to the fact that the boiling test for albumen is more often employed than the nitric acid (cold) test. It must be remembered, however, that in true Bence-Jones albumosuria the urine, if alkaline, should likewise not be expected to give any precipitate on heating until it has been rendered slightly acid, e.g. by the addition of acetic acid. The case described by Dr. Ter-Grigorianz (Hoppe-Seyler's 'Zeit. f. Phys. Chemie,' Strassburg, vol. vi, p. 537) was certainly not an example of Bence-Jones albumosuria. He specially stated that no precipitate occurred on boiling the urine with or without the addition of acetic acid.

January, 1846. The condition of the bones at the necropsy was regarded as a kind of osteomalacia, but Dalrymple, who made a microscopical examination of two vertebræ and a rib, found that the process somewhat resembled malignant disease. Kahler was the first to suggest that the bone disease in this case was really, as in his own case, multiple myeloma.

No. 2. *The case of Doornik, Stokvis, and Kühne.*—(W. Kühne, "Ueber Hemialbumose im Harn," 'Zeitschrift für Biologie,' 1883, vol. xix, p. 209.)

The patient was a man aged 40, under the care of Dr. Merkus Doornik, of Amsterdam. He fell ill November, 1868, and died August, 1869, but it was not till many years later that notes of the case and an account of the characters of the urine were reported by Kühne. There were remarkable nervous symptoms, and the clinical diagnosis was acute osteomalacia of the spinal column with compression of the spinal cord; no post-mortem examination, however, was made. The Bence-Jones proteid in the urine of this case appeared late in the disease, and was not present during the last three months of the patient's life.

No. 3. *The case of Kahler and Huppert.*—(O. Kahler, "Zur Symptomatologie des Multiplen Myeloms: Beobachtung von Albumosurie," 'Prager medicinische Wochenschrift,' 1889, vol. xiv, p. 33. H. Huppert, "Ein Fall von Albumosurie," *ibid.*, p. 35.)

The patient was a medical man (Dr. Loos) aged 46, when the disease first showed itself in July, 1879. He suffered from severe pains, progressive kyphosis, and became deaf; the duration of the illness was eight years, therefore much longer than in the other cases yet known. The Bence-Jones proteid was present in the urine during the last six years. He died in August, 1887. From the post-mortem examination Kahler identified the bone disease with the "multiple myeloma" of von Rustizky

and Zahn, and suggested that Case No. 1 and Case No. 2 were likewise of the same nature. Though the clinical diagnosis had been osteomalacia, Kahler pointed out that in future the presence of the Bence-Jones proteid in the urine might help to distinguish cases of multiple myeloma from osteomalacia. It is owing to the light thrown on the subject by Kahler's communication that Bozzolo and certain subsequent Italian writers have named this form of disease "*Malattia di Kahler*." In Kahler's case the spleen was enlarged and the inguinal lymphatic glands on both sides were affected, and in connection with my recent case it is worth mentioning that the free edge of the mitral valve of the heart was found thickened.

No. 4. *The case of Stokvis, Ribbink, and Zeehuisen*.—(B. I. Stokvis, '*Nederl. Tijdschrift voor Geneesk.*,' 1891, vol. ii, p. 36. H. C. G. Ribbink's '*Dissertation*,' Amsterdam, 1892. H. Zeehuisen, '*Nederl. Tijdschrift voor Geneesk.*,' 1893, vol. i, p. 829.<sup>1</sup> See also abstracts in '*Maly's Jahresbericht für Thier-Chem.*,' vol. xxi, p. 412; vol. xxii, p. 525; vol. xxiii, p. 577.)

The patient was a man aged 39. During life there was Bence-Jones proteid in the urine, and this body was detected likewise in the fæces. After death a diffuse change in the bones was found, which was regarded as "*osteo-sarcomatosis*." There were likewise tumours of the serous membranes and of other parts of the body, but whether in any way connected with the bone disease is uncertain. "*Calcareous metastases*" were observed in the kidneys, such as Virchow has drawn attention to as sometimes occurring in cases of malignant tumours of bones.

No. 5. *The case of Raschkes*.—(A. Raschkes, "*Ein Fall von seniler Osteomalacie mit Albumosurie*," '*Prager*

<sup>1</sup> There have been several articles on Bence-Jones albumosuria in Dutch journals. The literature of the subject was summed up by Tanja in '*Geneesk. Bladen*,' 1901, No. xi. *Vide* also Case No. 26.

med. Wochenschrift,' December 20th, 1894, No. 51, p. 649.)

The patient was a woman aged 65, with great tenderness of all the bones to percussion, especially over the sternum, ribs, lumbar vertebræ, and hips. After a few weeks in the hospital she died of pneumonia. At the necropsy the diagnosis of the bone disease was "senile osteomalacia of the thorax" and "senile osteoporosis of humerus and femur," but in the light of recent cases it is probable that the case should be regarded as one of multiple myeloma. The urine contained albumen as well as Bence-Jones proteid, and the presence of chronic interstitial nephritis as a complication was confirmed by the post-mortem finding.

No. 6. *The case of Professor Stintzing, of Jena.*—(Seegelken, "Ueber Multiples Myelom und Stoffwechsel Untersuchungen bei derselben," 'Deut. Archiv für klin. Med.,' 1897, vol. lviii, p. 276. M. Matthes, "Ueber Eiweisskörper im Urine bei Osteomalacie," 'Verhandl. des XIV Congresses für innere Medicin,' 1896, p. 476. R. Neumeister, 'Lehrbuch der physiol. Chemie,' 1897, second edition, p. 804.)

The patient was a man aged 61, supposed to have osteomalacia, admitted to Stintzing's Clinic in September, 1895. The urine was studied by Matthes in Neumeister's laboratory. Death occurred in July, 1896. Seegelken termed the new growth which was found in the bones at the necropsy "chondrosarcoma." It may be noted with reference to the case described in the present paper that Stintzing's patient had suffered from articular "rheumatism" eight years before his fatal illness.

No. 7. *Senator's case.*—(H. Rosin, "Ueber einen eigenartigen Eiweisskörper in Harne und seine diagnostische Bedeutung," 'Berliner klin. Wochenschr.,' 1897, p. 1044. H. Senator, "Asthenische Lähmung, Albumosurie, und multiple Myelome," 'Berliner klin. Wochenschr.,' 1899,

p. 161. The urine has likewise been studied in Süssmann's 'Dissertation,' Leipzig, 1897.)

The patient, a woman aged 36, was first seen in February, 1897, and died in April of the same year. The case was complicated by a renal affection, and by a remarkable nervous affection regarded by Senator as asthenic bulbar paralysis (myasthenia gravis).

No. 8. *Bozzolo's case*.—(Camillo Bozzolo, "Sulla Malattia di Kahler," in the 'Transactions of the Eighth Medical Congress,' Naples, October, 1897; and in 'La Clinica Medica Italiana,' Milan, January, 1898, p. 1. Referred to also in 'Centralblatt für die med. Wissenschaft,' 1898, vol. xxxvi, p. 572.)

The patient was a native of Como, aged 42, the proprietor of an hotel in London, where he had suffered from pain in one loin and was reported to have albuminuria. Amongst the symptoms mentioned are pains in the vertebral column and ribs, curvature of the spinal column, and signs of pressure on the spinal cord (increased knee-jerks, etc.). His illness had probably lasted two years at least before Bozzolo saw him at Turin, where the examination of the urine by Bozzolo's assistant, Belfanti, showed that the case was not one of ordinary albuminuria. On heating the urine a precipitate commenced to form at about 45° C., and continued to increase till the temperature of 55° C. was reached, but dissolved up again on boiling. No necropsy is recorded.

No. 9. *The case of Lichtheim and Ellinger*.—(A. Ellinger, "Das Vorkommen des Bence-Jones'schen Körpers im Harn bei Tumoren des Knochenmarkes und seine diagnostische Bedeutung," 'Deut. Archiv für klin. Medicin,' 1899, vol. lxii, p. 255.)

The patient was a man aged 45, who was admitted to the Königsberg Clinic in October, 1897, and died in December of the same year. This case was complicated by jaundice and considerable fever. The urine, besides

the Bence-Jones proteid, contained a trace of albumen and a few hyaline casts. The spinal cord showed degenerative changes in the posterior columns. The changes found in the bones at the necropsy were regarded as diffuse lymphoid infiltration together with multiple lymphomatous tumours. After death the presence of Bence-Jones proteid was thought to have been proved in a piece of rib, and in some of the blood and ascitic fluid.

No. 10. *Bradshaw's case*.—(T. R. Bradshaw, "A Case of Albumosuria in which the Albumose was spontaneously precipitated," 'Med.-Chir. Trans.,' London, 1898, vol. lxxxi, p. 259. Bradshaw and Warrington, "The Morbid Anatomy and Pathology of Dr. Bradshaw's Case of Myelopathic Albumosuria," *ibid.*, 1899, vol. lxxxii, p. 251. Bradshaw, 'Trans. Path. Soc.,' London, 1900, vol. li, p. 140. Bradshaw, "Myelopathic Albumosuria," 'Brit. Med. Journ.,' November 3rd, 1900, p. 1304. Bradshaw, "Myelopathic Albumosuria," 'Lancet,' October 4th, 1902, p. 929.)

A man aged 70 noticed in 1896 that his urine was sometimes "milky." In 1897 Dr. Bradshaw found that Bence-Jones proteid was constantly present in the patient's urine, and regarded the occasional milkiness as due to spontaneous precipitation of this proteid. The nature of the bone affection was therefore diagnosed during life, and this diagnosis was confirmed by an incomplete post-mortem examination after the patient's death in August, 1898. The kidneys showed a certain amount of interstitial fibrosis.

No. 11. *Case of Naunyn and Magnus-Levy*.—(Naunyn, "Ein Fall von Albumosurie," 'Deut. med. Wochenschrift,' 1898, Vereins-Beilage, p. 217. A. Magnus-Levy, "Ueber den Bence-Jones'schen Eiweisskörper," Hoppe-Seyler's 'Zeitschrift für phys. Chemie,' 1900, vol. xxx, p. 200.)

No necropsy was made. In this case, according to Naunyn, a spontaneous precipitation of Bence-Jones pro-



teid occurred in the urine on standing. Magnus-Levy, who carefully studied the urine, found that the daily excretion of the proteid in question often reached 36 grammes.

No. 12. *The first case of Dr. Fitz.*—(R. H. Fitz, "The Significance of Albumosuria in Medical Practice," 'American Journ. Med. Sci.,' 1898, vol. cxvi, p. 30.)

The patient, a woman aged 53, was first seen in November, 1895. The clinical diagnosis was myxoedema, and she died in April, 1896, whilst under treatment with thyroid extract. The urine was examined by Dr. E. S. Wood, but owing to there being no post-mortem examination, myelomatous bone disease cannot be excluded.

No. 13. *The second case of Dr. Fitz.*—(R. H. Fitz, loc. cit., p. 42. J. H. Wright, "A Case of Multiple Myeloma," 'Johns Hopkins Hospital Reports,' 1900, vol. ix, p. 359; also 'Journ. of the Boston Society of Med. Sci.,' 1900, vol. iv, p. 195.)

The urine was examined by Dr. E. S. Wood. The whole case and necropsy are recorded by Wright. The patient, at first under the charge of Dr. F. C. Shattuck, was a man aged 54, admitted to the Massachusetts General Hospital in February, 1898, where he died in July of the same year. In this case there were nervous symptoms, including diplopia, and some incontinence of urine. A fairly good history of syphilis was obtained. The Röntgen rays are stated to have been of great service in facilitating the recognition of the bone lesions.

No. 14. *The case of Buchshtab and Schaposchnikow.*—(L. Buchshtab and B. Schaposchnikow, "Diffuses Myelom der Rumpfknochen mit einer Typischen Albumosurie," abstract in German in 'St. Petersburger med. Wochenschrift,' 1899, from 'Russ. Arch. Pat., Klin. Med., Bact.,' vol. vii; also abstract in 'Centralblatt für allg. Pathologie,' 1899, vol. x, p. 589.)

The patient was a man aged 42, in the Israelitish Hospital at Odessa. The diagnosis of myelomatosis was made during life owing to the finding of Bence-Jones proteid in the urine. It was confirmed by the necropsy. In this case the symptoms of a "compression-myelitis" developed owing to tumours projecting into the spinal canal; swellings appeared on the ribs, and there was a large growth connected with the right iliac bone.

No. 15. *D'Allocco's case*.—(D'Allocco, "Sulla Malattia di Kahler," at the tenth Medical Congress, Rome, October, 1899, 'Arch. Ital. di Medicina Interna,' 1900, vol. iii, fasc. Nos. 1 and 2; referred to also by U. Flora in his article, "Sulla Malattia di Kahler," 'Rivista Critica di Clinica Medica,' Florence, 1900, Nos. 46 and 47.)

A man aged 44 commenced to suffer from a painful and deforming bone disease after a fall on his chest. There was constant Bence-Jones albumosuria, and death occurred in five months. Diffuse myelogenic sarcoma was the post-mortem anatomical diagnosis of the bone disease. Chronic nephritis was likewise diagnosed. In this case a spontaneous precipitate (supposed to be of Bence-Jones proteid) was noted in the urine. Tube-casts were also found, and the necropsy confirmed the existence of chronic nephritis as a complication. D'Allocco thinks that he demonstrated the presence of the Bence-Jones proteid in the patient's blood.

No. 16. *The case of Lichtheim and Askanazy*.—(S. Askanazy, "Ueber die diagnostische Bedeutung der Ausscheidung des Bence-Jones'schen Körpers durch den Harn," 'Deut. Archiv für klin. Medicin,' 1900, vol. lxxviii, p. 34.)

The patient was a man aged 51, in Professor Lichtheim's Clinic at Königsberg. The amount of Bence-Jones proteid in the urine was only  $\frac{1}{2}$  to  $1\frac{1}{2}$  per mille. Askanazy apparently succeeded in extracting a proteid identical with that in the urine from a portion of the

patient's bone-marrow obtained at the necropsy. The man certainly had lymphatic leucocythæmia, and Askanazy thinks that the bone disease was only part of the leucocythæmia. Possibly, however, the disease may have been a "mixed" form of multiple myeloma; that is to say, it may have been an example of the association of the two types of multiple myeloma to which I have previously referred—namely, a "lymphatic" type leading, in this instance, to lymphatic leucocythæmia,<sup>1</sup> and a type similar to that of my second case (patient J. T—), giving rise to Bence-Jones albumosuria. The latter form of myelogenic growth may have been still in an early stage of development, and may have escaped notice amidst the "lymphatic" growth at the post-mortem examination. This might likewise account for the relatively small amount of Bence-Jones proteid in the patient's urine.

No. 17. *Latzko and Sternberg's case*.—(M. Sternberg, in "Vegetationsstörungen und Systemerkrankungen der Knochen," Nothnagel's 'Spec. Path. u. Therapie,' 1899, vol. vii, part ii, division 2, p. 57.)

The patient was a woman aged 56, whom Sternberg saw with Dr. W. Latzko in November, 1897. She had been ill two years with pains in the bones, etc. Bence-Jones proteid in great quantity was found in the urine by Dr. E. Freund. Death occurred several months later, but no post-mortem examination could be made.

No. 18. *Barr's case*.—(J. Barr, "Case of Myelopathic Albumosuria," 'Liverpool Med.-Chir. Journal,' March, 1901, p. 23.)

The patient was a man aged 53. There were pains in

<sup>1</sup> A. Pappenheim has endeavoured to explain the fact of lymphatic leukaemia occasionally supervening on pseudo-leukaemia in 'Virchow's Archiv,' 1901, vol. clxvi, p. 473. See also the elaborate summary of his views regarding the relations of lymphocytes to plasma-cells, etc. ("Weitere kritische Ausführungen zum gegenwärtigen Stand der Plasmazellen Frage"), in 'Virchow's Arch.,' 1902, vol. clxix, pp. 372—428.

the spinal column, a swelling in the manubrium sterni, etc. The bone disease seemed to be of progressive character. Barr found the quantity of urine usually between forty and sixty ounces daily, and it rarely contained less than twelve per mille of the Bence-Jones proteid. I understand that no post-mortem examination was made. In connection with my own recent case it is interesting to note that Dr. Barr's patient presented undoubted signs of cardiac valvular disease.

No. 19. *The case of a French physician.*—(T. R. Bradshaw, "On the Evolution of Myelopathic Albumosuria," 'Brit. Med. Journ.,' July 13th, 1901, p. 75. Obituary notice on Dr. P. F. Colrat, 'Brit. Med. Journ.,' September 7th, 1901.)

The patient was a well-known French physician of Lyons, aged 55. The Bence-Jones proteid first appeared in the urine in December, 1899; the amount was at first very little, but it gradually increased and ultimately reached a maximum proportion of ten per mille. Death occurred from pneumonia in August, 1901. In this case Bradshaw ('Lancet,' October 4th, 1902, p. 931) says he observed a semi-fluctuating swelling of about the size of a large hen's egg in connection with one of the ribs.

No. 20. *The case of Iglehart, Hamburger, and Simon.*—(L. P. Hamburger, "Two Examples of Bence-Jones Albumosuria associated with Multiple Myeloma," 'Johns Hopkins Hospital Bulletin,' February, 1901, p. 38. C. E. Simon, "Observations on the Nature of the Bence-Jones Albumen," 'American Journ. Med. Sci.,' June, 1902, p. 939.)

The patient was a lady aged 49, whose first symptom was a sharp pain over one of the ribs in August, 1900. The examination of the urine led to the clinical diagnosis of multiple myeloma. Spontaneous fracture of the left femur occurred a few days before the patient's death in August, 1901. No necropsy was made.

No. 21. *The case of Osler, Hamburger, and MacCallum.*—(Hamburger, loc. cit. W. G. MacCallum, "A Case of Multiple Myeloma," 'Journ. Experimental Medicine,' 1901, vol. vi, p. 53.)

The patient was a coloured woman aged 50, admitted to the Johns Hopkins Hospital in October, 1900. The urine contained Bence-Jones proteid, and the clinical diagnosis of multiple myeloma was confirmed by the necropsy findings recorded by MacCallum.

No. 22. *Kalischer's case.*—(S. Kalischer, "Ein Fall von Ausscheidung des Bence-Jones'schen Eiweisskörper," 'Deut. med. Wochenschr.,' 1901, No. 4, p. 54.)

The patient was a woman aged 67. In this case a spontaneous precipitate (supposed to be of the Bence-Jones proteid) was observed in the urine on allowing it to stand for a long time. After death, examination of the ribs showed a tumour-like hyperplasia of the bone-marrow. Professor Loewy failed to detect the presence of Bence-Jones proteid in the bone-marrow from the ribs and humerus. It may be noted that one of the patient's daughters had died at the age of thirty of "pernicious anæmia."

No. 23. *Rostoski's case.*—(O. Rostoski, "Albumosurie und Peptonurie," at the meeting of the Phys.-med. Ges. zu Würzburg, June 13th, 1901, reported in the 'Sitzungs-Berichte,' 1901, Nos. 2 and 3; abstract in 'Muenchener med. Wochenschrift,' July 2nd, 1901.)

Rostoski gives no details of this case, but from the results of his examination of the urine, says that he inclines to the view of Magnus-Levy, that the Bence-Jones proteid (at least, what he found in his case) is not to be classed as an albumose. He has likewise recorded certain investigations regarding the Bence-Jones body in his paper "Zur Kenntniss der Präcipitine" (Würzburg, 1902).

No. 24. *The case of Jochmann and Schumm.*—(G. Joch-

mann and O. Schumm, "Typische Albumosurie bei echter Osteomalacie," 'Muenchener med. Wochenschrift,' August 20th, 1901, p. 1340; and "Zur Kenntniss des Myeloms und der Sogenannten Kahler'schen Krankheit," 'Zeitschrift für klin. Medicin,' 1902, vol. xlv, p. 445.)

The patient was a woman aged 37, who was admitted to the Hamburg-Eppendorf Hospital in November, 1900. Her illness commenced with pains in the hips. Afterwards she suffered from pains in the loins and sternum, progressive kyphosis, spontaneous fractures of the thigh-bones, and increasing debility. She died from pneumonia, one and a half years after the commencement of the illness. During the last weeks of life her urine contained a considerable quantity of Bence-Jones proteid. She likewise had nephritis and hæmorrhagic glaucoma. After death an albumose-like body was detected in the blood. Though the authors originally considered that the case was one of genuine osteomalacia, their description of the post-mortem examination gave rise to considerable doubt as to the correctness of their view. Dr. T. R. Bradshaw, in a short communication on the subject ('Muenchener med. Woch.,' February 4th, 1902, p. 191), enumerated the main objections to the acceptance of their pathological inferences, and the authors afterwards republished the case as one of multiple myeloma. It should be noted that in this case the pelvis and long bones were affected, as well as the ribs and vertebral column.

No. 25. *Donetti's case*.—(E. Donetti, "Sulla Malattia di Kahler," 'Rivista Critica di Clinica Medica,' Florence, 1901, No. 46, p. 789.)

The patient was a man aged 45, with a painful affection of the bones, especially of the vertebral column and ribs, with anæmia, and with Bence-Jones proteid constantly in his urine. The method of D'Allocco seemed to demonstrate the presence of Bence-Jones proteid in the blood (compare Case No. 15).

No. 26. *The case of Hijmans van den Bergh, of Rotter-*

*dam.*—(A. Grutterink and C. J. de Graaff, "Ueber die Darstellung einer Krystallinischen Harnalbumose," Hoppe-Seyler's 'Zeitsch. für phys. Chemie,' 1902, vol. xxxiv, p. 393. A. A. Hijmans van den Bergh, "Albumosurie," reprinted from 'Herinnerungs-Bundel Prof. Rosenstein,' 1902.)

The patient, a manservant aged 36 years, had enjoyed good health till September, 1900, when he was seized with pain on the left side of the chest. Afterwards he had pains on the right side of the chest, in the right shoulder, and in the back. He had to give up work, and was admitted into the Rotterdam Hospital in March, 1901. In the hospital great deformity of the thorax occurred from progressive bending of the vertebral column and sternum, and death took place in December, 1901. At the necropsy the bone-marrow of vertebræ, sternum, and ribs was found transformed into a sarcoma-like growth. A femur was examined and found similarly affected, but in a lesser degree. The liver was fatty, and the kidneys showed slight interstitial changes. Miss Grutterink and Miss de Graaff succeeded in obtaining the Bence-Jones proteid in a crystalline form from the urine of this case. I have to thank Dr. Bradshaw for kindly placing a copy of Dr. Hijmans van den Bergh's paper at my disposal.

No. 27. *Conti's case.*—(Pietro Conti, "Albumosuria e Neoplasie Sistematiche delle Ossa," 'La Clinica Medica Italiana,' Milan, 1902, pp. 211—247.)

The patient was a lady aged 60, whose first symptoms were costal pains in August, 1899, when she was at the health resort of Mont-Dore on account of bronchial catarrh. She died October 30th, 1901, after about twenty-six months of suffering. The symptoms of the skeletal disease were chiefly referable to the bones of the trunk—pains connected with the ribs, sternum, and spinal column; kyphosis; and little tumours on the sternum and right ilium. There was cachexia, and

towards the end the muscular weakness was extreme. Bence-Jones proteid was first detected in the urine in November, 1900. For several weeks prior to the death of the patient, the urine is said to have contained albumen, but no longer any Bence-Jones proteid; it likewise contained hyaline and a few granular casts. Unfortunately no post-mortem examination was made. I am indebted to Dr. A. E. Garrod for drawing my attention to Conti's publication.

No. 28. *The present case.*—(Abstract already given.)

UNCERTAIN CASES, AND CASES IN WHICH THE REACTIONS OF THE  
PROTEID IN THE URINE WERE NOT QUITE CHARACTERISTIC.

No. 29.—Dr. Sidney Martin (discussion on Dr. Bradshaw's paper, 'Proceedings of the Royal Med. and Chir. Soc.,' 1898, third series, vol. x, p. 120) referred to the case of a woman under the care of Dr. H. R. Spencer, at University College Hospital, for an ovarian tumour, which was removed. The urine, sometimes milky from precipitation of the proteid, was examined by Dr. Sidney Martin, who states that it contained "the same body or bodies" as those referred to by Dr. Bradshaw in his case. The subsequent history of the case is not given.

No. 30.—Dr. R. Hutchison (discussion on the "Proteids in Urine," 'Trans. Path. Soc.,' London, 1900, vol. li, p. 146) referred to a man who died in the London Hospital with multiple tumours of bones (extremities, ribs, and vertebræ). A flocculent precipitate separated out from the urine at 58° C., but did not re-dissolve on boiling. In this respect, and in its behaviour to nitric acid, the substance present in the urine had not quite the characteristic reactions of Bence-Jones proteid. The case should certainly, however, be mentioned here. Dr. Hutchison kindly informs me that the patient was 38 years old and



died within a week of admission. The upper end of one humerus, preserved in the London Hospital Museum, is much enlarged by a very vascular growth. Sections from one of the growths show it to consist chiefly of rather large rounded or polygonal cells with a good deal of protoplasm around a medium-sized nucleus. The protoplasm of many of the cells, Dr. Hutchison tells me, contained granules, possibly of the same nature as those in the tumour-cells of my case, J. T—.

No. 31.—Dr. Lee Dickinson (discussion on the “Proteids in Urine,” ‘Trans. Path. Soc.,’ London, 1900, vol. li, p. 170) mentioned a case of leucocythæmia in the practice of Mr. Edgecombe Venning, in which Bence-Jones proteid—or, at all events, a proteid coagulating like Bence-Jones proteid at a relatively low temperature—occurred in the urine, and in which no other disease but leucocythæmia could be found.

SUPPOSED CASES WHICH HAVE BEEN INCORRECTLY INCLUDED  
IN SUMMARIES OF BENCE-JONES ALBUMOSURIA CASES.

No. 32.—A case described by Byrom-Bramwell and Noel-Paton (“On a Crystalline Globulin occurring in Human Urine,” ‘Reports from the Laboratory of the Royal College of Physicians,’ Edinburgh, 1892, vol. iv, p. 47) was at one time regarded by Huppert (“Ueber einen Fall von Albumosurie,” ‘Hoppe-Seyler’s Zeitschrift für phys. Chemie,’ vol. xxiii, p. 500) as an instance. But after himself examining the proteid from the urine in question, he altered his mind (“Ueber den Noel-Paton’schen Eiweisskörper,” ‘Centralblatt f. d. med. Wiss.,’ July 9th, 1898, p. 481) and regarded the substance as a globulin. The case is remarkable for the spontaneous precipitation of the proteid in crystalline form on allowing the urine to stand for a longer or shorter period, sometimes a day or two, sometimes weeks or months.

No. 33.—Simon ('Amer. Journ. Med. Sci.,' June, 1902, p. 954) wrongly cites a case reported by Karl Ewald ("Ein chirurgisch-interessanter Fall von Myelom," 'Wiener klin. Wochenschrift,' 1897, p. 169). The patient was a man aged 62. The diagnosis of myeloma was made during life owing to the examination of part of a growth removed from the right clavicle in April, 1894. Death occurred in May of the same year. No necropsy is recorded, and Bence-Jones proteid is not said to have been found in the urine. The case, therefore, cannot be accepted as an example of multiple myeloma with Bence-Jones albumosuria, although Jochmann and Schumm ('Zeitschr. f. klin. Med.,' 1902, vol. xlv, p. 467), as well as Simon, have referred to it as such.

No. 34.—A supposed case of Dr. Vladimir de Holstein ('Semaine Médicale,' 1898, p. 206, and 1899, p. 83) is likewise referred to by Simon (loc. cit., p. 955), who states that the diagnosis of "multiple myelomatosis" was made during life owing to the state of the urine, and that the diagnosis was confirmed by a subsequent necropsy. However, on looking up Simon's references, I could only find a notice of Bradshaw's case, and a short *résumé* of the subject by Dr. V. de Holstein, but no new case.

In conclusion, I must express my thanks to those who have so kindly helped me in this account, only a small part of which I can fairly call my own. Besides Dr. R. Hutchison and Dr. J. J. R. Macleod, I have already mentioned a number of those to whom I am indebted for assistance: Professor R. Muir, of Glasgow, for his report on the tumour tissue and for other information; Dr. J. M. H. MacLeod and Dr. Gustav Mann, in regard to the examination of some of the tumour-cells; Dr. F. E. Batten, for examination of the nervous tissues; and Dr. J. H. Drysdale, for examination of the blood. Mr. S. G. Shattock has helped me very much in the pathological examination

of the skeleton and viscera, and Dr. A. E. Garrod in the examination of the urine. I must likewise thank Dr. Dengler, the house physician during the time that the patient was in the hospital, for the trouble he has taken in connection with the case; and my colleague, Dr. J. P. zum Busch, for kindly allowing me to use the photograph of the spinal arthropathy patient for comparison. To Dr. T. R. Bradshaw, of Liverpool, I am not only indebted for his published works on the subject; he took the trouble of coming to the German Hospital specially to examine the patient, and owing to his previous experience he was able to give valuable confirmation to the diagnosis. Through his kindness, moreover, I have previously become acquainted with some of the reactions of the Bence-Jones proteid in urine, for owing to some correspondence in regard to my previous case of multiple myeloma, he sent me in June, 1898, a bottle of characteristic urine from the patient he then had under observation (Case No. 10 in the Summary). I have also to thank Mr. Shiells for his care in the coloured drawing of the tumour.

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## APPENDIX.

### ADDITIONAL CASES OF BENCE-JONES ALBUMOSURIA.

Dr. J. M. Anders and Dr. L. N. Boston, of Philadelphia, have recently published<sup>1</sup> notes of three cases of Bence-Jones albumosuria.

CASE A.—A well-developed man, aged 32, fond of athletics. He had had malaria at the age of twenty. In September, 1900, he had a severe fall, and afterwards complained of soreness in the dorsal and lumbar regions.

<sup>1</sup> "Bence-Jones Albumosuria," *'Lancet,'* January 10th, 1903, p. 93.

In November of the same year he suffered from an attack of herpes zoster on the right side, and he noticed that he was thirsty; at this time he was voiding 2900 c.c. urine in the twenty-four hours. In 1901 he complained of repeated attacks of pain, and what he described as feelings of "giving way" in the bones. Tumours appeared over one of the ribs, on the right femur, and behind the right tonsil. There was frequent and copious epistaxis. Examination of the blood showed a certain degree of anæmia. Vision was impaired, and L. W. Fox found definite ophthalmoscopic changes present: hæmorrhages, and white spots in the retina, and choked disc. The patient died on April 22nd, 1901, but no necropsy was permitted. In this case albumen was present in the urine together with the Bence-Jones body. The total proteid measured 2 to 3 per mille by Esbach's method, and the daily amount of urine was about 2900 c.c. No tube casts were ever detected.

CASE B.—A man aged 43 years, of temperate habits, with a family history of gout, rheumatism, and severe headaches. He was seen for the first time by Dr. Anders in November, 1901. One year ago he had suffered during three weeks from acute articular rheumatism.<sup>1</sup> Three years ago he fractured his right leg in a bicycle accident. In January, 1901, he was thought to have nephritis, and afterwards rapidly lost weight and strength, suffering likewise from pains in the extremities and back, and severe attacks resembling hemicrania. Examination of the blood showed deficiency in hæmoglobin and red cells. Retinal hæmorrhages were detected in both eyes. The patient died in 1902, but a necropsy could not be obtained. In this case the daily quantity of urine was 2500 c.c., but later on only 1875 c.c. The total proteid never exceeded 2·33 per mille by Esbach's method; during the last month of life, however, it was much reduced, and a reaction for

<sup>1</sup> In regard to the question of acute rheumatism, compare the post-mortem findings in the heart of my case J. T.—

the Bence-Jones body could no longer be obtained.<sup>1</sup> No tube casts were seen.

CASE C.—A man aged 33 years, with a family history of gout, rheumatism, and Bright's disease. Six years ago, when he applied for life assurance, albumen and casts were detected in his urine. On examination in October, 1900, moderate enlargement of the left ventricle of the heart was made out. The retinal changes of chronic interstitial nephritis were found present in the right eye, but not in the left. There was some emaciation and anæmia. When the patient was last seen the disease seemed not to have made much progress. The urine (daily quantity, 2300 c.c.) was of specific gravity 1008—1012, and contained albumen. By Esbach's tube the total amount of proteid was estimated at only one tenth to three tenths per mille. The presence of the Bence-Jones body, as well as the albumen, was first ascertained in October, 1901, but it did not become a constant constituent till recently. Hyaline, granular, and the so-called amyloid casts were detected in the urine whenever searched for.

In their review of the subject, Dr. Anders and Dr. Boston speak of symptoms having been present in certain percentages of the cases, but it is not clear which cases these authors have admitted as genuine ones of Bence-Jones albumosuria. They allude to thirty cases which they have collected from the literature, but amongst them they seem to have included several in which there is no evidence that any albumosuria was present. The case of Professor R. von Jaksch, to which they refer, was shown at the Society of German Physicians in Prague on December 2nd, 1892. The patient was a woman with typical symptoms of Graves' disease, and with a swelling of the lower extremities which Jaksch thought might be of myxœdema-

<sup>1</sup> See Case No. 2 in my Summary of Cases.

tous nature; but no albumosuria was reported.<sup>1</sup> They quote K. Ewald's case of myeloma,<sup>2</sup> in the account of which there is no record of the Bence-Jones body, or of any albumose being detected in the urine. They have apparently likewise included H. F. Vickery's case<sup>3</sup> of "pseudo-leukæmia" in a patient aged 19 years, whose urine contained the "slightest possible trace of albumen," but nothing of the nature of the Bence-Jones body. Nor was any kind of albumosuria reported in either of the patients of J. H. Musser,<sup>4</sup> to whom they refer as having published a case. The case of Dreschfeld and Milroy, which they quote, had, however, escaped me.

CASE D.—(J. A. Milroy, "A Contribution to our Knowledge of a Rare Form of Albumose occurring in the Urine," 'Journal of Pathology,' Edinburgh and London, 1901, vol. vii, p. 95.)

The man was an in-patient at the Manchester Infirmary twice during the year 1898, but his subsequent history is not known. Dr. Dreschfeld's notes point to there being new growths in the ribs and vertebræ. A hard painless growth was observed on one of the lower ribs on the right side. Milroy's paper discusses the nature and reactions of the Bence-Jones body in the urine.

CASE E.—Sir Lauder Brunton kindly informs me that Dr. David Young, of Rome, had a case of Bence-Jones

<sup>1</sup> See report of the case in 'Prager medicinische Wochenschrift,' 1892, vol. xvii, p. 602.

<sup>2</sup> 'Wiener klinische Wochenschrift,' 1897, p. 169. See Case No. 33 of my Summary of Cases.

<sup>3</sup> "Pseudo-leukæmia with Chronic Relapsing Fever," 'International Clinics,' twelfth series, 1902, vol. ii, p. 89.

<sup>4</sup> "Note on the Fever of Hodgkin's Disease," 'American Medicine,' January 4th, 1903, p. 13. In this paper Musser describes two cases, one of which he regards as an example of Hodgkin's disease with tuberculosis, the other as "so-called Hodgkin's disease in which the clinical course was that of tuberculosis," and in which tubercle bacilli were present in the sputum. In neither of these cases was any albumosuria recorded.

albumosuria in which on precipitating the Bence-Jones proteid in the urine with alcohol the precipitate seemed to equal the height of one third of the whole mixture. There was probably no post-mortem examination in this case.

CASE F.—(O. Langendorff and J. Mommsen, "Beiträge zur Kenntniss der Osteomalacie," 'Virchow's Archiv,' 1877, vol. lxi, pp. 452—487.)

I have to thank Professor Bäumler, of Freiburg, in Baden, for drawing my attention to this case, which was perhaps one of multiple myeloma with Bence-Jones albumosuria, though at the time regarded as one of osteomalacia only. The patient, a tailor aged 38 years, began to have "rheumatic pains" in 1869, and, about four years later, he frequently suffered from fractures of bones without any considerable violence to account for them. His thorax became deformed, and he died during an attack of dyspnoea, October, 1875, in the clinic of Professor Czerny, of Freiburg. The cysts found in the bones of this case might perhaps have been due to hæmorrhages in connection with myelomatous growth. The urine was thought to contain a small amount of Bence-Jones proteid.

CASE G.—P. Vignard and L. Gallavardin ("Du Myélome Multiple des Os avec Albumosurie," 'Revue de Chirurgie,' Paris, 1903, No. 1, p. 91) record the case of a man aged 56 years, who was admitted September, 1899, to the Hôtel Dieu, of Lyons, suffering from severe thoracic pains and cachexia. He died in a comatose condition a few days after admission. The necropsy showed multiple myeloma of the bones of the thorax, but there is no proof that any Bence-Jones proteid had been present in the urine (nitric acid had only given a slight precipitate).

CASE H.—Dubost ('Thèse de Paris,' quoted by Vignard and Gallavardin, loc. cit.) gives the case of a man aged 46 years, who died in a collapsed condition, December,

1896, soon after admission to a hospital in Lille. The necropsy showed multiple tumours of the ribs, sternum, and vertebræ, doubtless a form of multiple myeloma. During life the chief symptoms had been severe lumbar pains and rapid cachexia. The urine was stated to contain 3·5 per mille albumen, but no special tests for the Bence-Jones proteid were employed.

CASE I.—C. E. Campbell-Horsfall ('Lancet,' 1903, vol. i, p. 1166) gives the case of a man in whom temporary Bence-Jones albumosuria was observed during several days after a severe gunshot injury to the leg, which necessitated immediate amputation. Recovery took place.

CASE K.—L. N. Boston ('American Journ. Med. Sciences,' April, 1903, p. 658) gives the case of a lady aged 50 years, whose left breast was removed in 1898 for supposed carcinoma, and who has been losing flesh and strength. In January, 1902, she had a severe fall, and six weeks later Bence-Jones proteid was first detected in the urine; it was absent, however, at some recent examinations. The patient likewise suffers from certain pains and paræsthesiæ.

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#### DESCRIPTION OF PLATES.

Multiple Myeloma (Myelomatosis) with Bence-Jones Proteid in the Urine (F. PARKES WEBER, M.D., F.R.C.P.).

PLATE I.—The patient J. T—, with multiple myeloma and Bence-Jones albumosuria, to illustrate the kyphosis (from a photograph taken in December, 1900).

PLATE II.—A patient with the kyphosis of spondylitis deformans (Pierre Marie's "spondylose rhizomélique") for comparison with the patient J. T— and Dr. Bradshaw's patient.



*Parkes Weber: Multiple Myeloma. Plate I.*



The patient, J. T—, with multiple myeloma and Bence-Jones albumosuria, to illustrate the kyphosis (from a photograph taken in December, 1900).



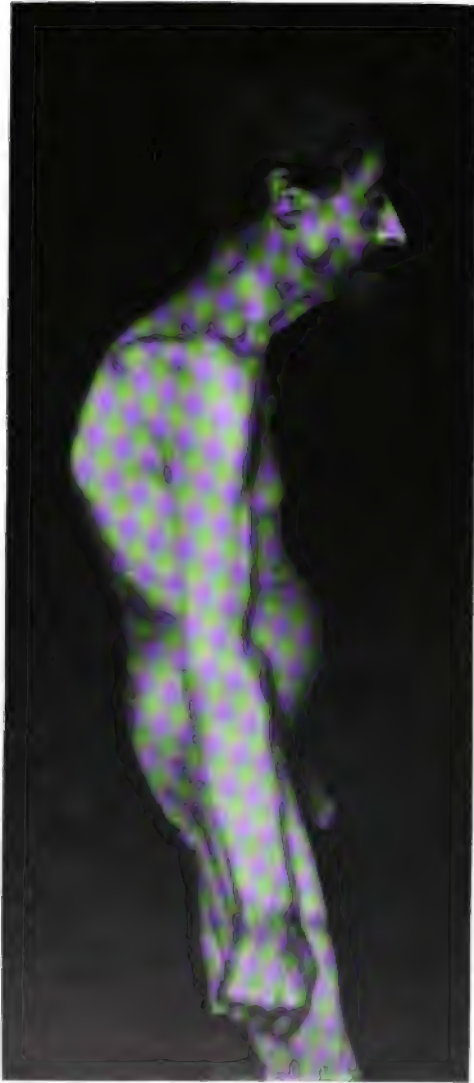
*Parkes Weber: Multiple Myeloma. Plate II.*



A patient with the kyphosis of spondylitis deformans (Pierre Marie's "spondylose rhizomélisque") for comparison with the patient J. T. and Dr. Bradshaw's patient.

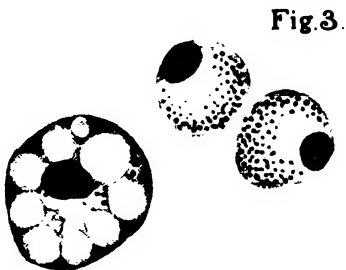
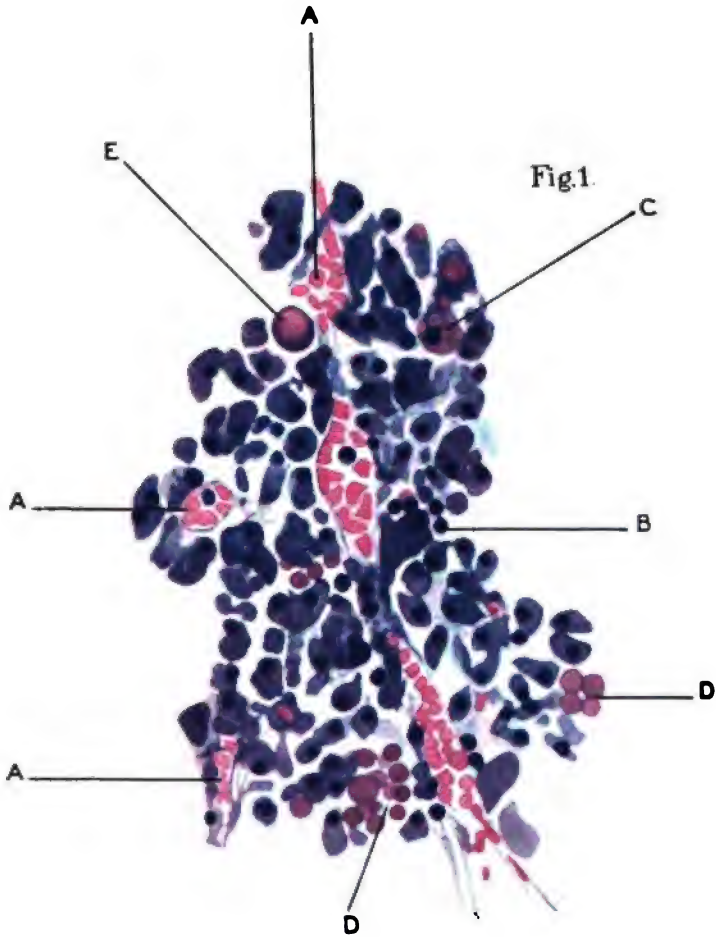


*Parkes Weber: Multiple Myeloma, Plate III.*



Dr. Bradshaw's patient (Case No. 10 in the Summary), with multiple myeloma and Bence-Jones albumosuria, to illustrate the kyphosis.





Showing colour-reaction of the granules and globules of the  
tumour-cells. (For description see end of paper.)





PLATE III.—Dr. Bradshaw's patient (Case No. 10 in the Summary) with multiple myeloma and Bence-Jones albumosuria, to illustrate the kyphosis. Reproduced by permission from Dr. Bradshaw's paper in the 'Med.-Chir. Transactions,' vol. lxxi.

PLATE IV.—To show colour reaction of the granules and globules of the tumour-cells.

FIG. 1.—Part of a section of the new growth (under oil immersion).  
A. Blood-vessel with thin walls filled with red blood-corpuscles.  
B. Cells resembling lymphocytes. C. Medium-sized globules in tumour-cell. D. Globules of various sizes free amongst the tumour-cells. E. Large globule, three or four times larger than a red blood-corpuscle, enclosed in a tumour-cell. The section was stained with hæmatoxylin after Mann's eosin and methyl-blue combination. The small granules in the tumour-cells are not seen. It will be observed that the globules, both those enclosed in tumour-cells and those lying free in the tissue, are stained differently to the red blood-corpuscles. In the big globule (E), however, the tint approaches more nearly that of the red corpuscles. The shape of the globules in question differs from that of the red blood-corpuscles in being almost perfectly spherical.

FIG. 2 (higher magnification).—A mulberry-like collection of globules, apparently formed in a single cell, of which the nucleus is visible.

FIG. 3.—Two tumour-cells showing granules and characteristic excentric position of the nucleus, which is surrounded by a zone free from granules; a larger tumour-cell containing granules and globules of various sizes. This figure is a semi-diagrammatic representation from a section sent me by Professor R. Muir, stained with Mann's eosin and methyl-blue combination without the additional hæmatoxylin which was employed in the preparations from which the first two figures were drawn.

## DISCUSSION

Dr. T. R. BRADSHAW said that scarcely five years had passed since he had had the honour of bringing his first case of myelopathic albumosuria to the notice of the Society. When his paper was written, at the close of 1897, not more than half a dozen cases which were probably of this nature were to be found in the whole range of medical literature, and the debate which followed indicated that the very existence of this disease was practically unknown to the profession in this country. A year after his first paper he had had the good fortune to be able to lay before the Society a fairly complete account of his case, not only in its clinical and chemical aspects, but also from the point of view of its morbid anatomy; and he put in a claim that myelopathic albumosuria should be recognised as a definite disease, distinct on the one hand from osteomalacia, and on the other from multiple tumours in the marrow, unattended by changes in the urine. He had also ventured to predict that when the existence of this disease came to be generally known its occurrence would be found to be less infrequent than it appeared to be. Whereas in 1899 he had been able to collect only eight cases, including his own, Dr. Weber now brought up the total number to thirty-two, and he himself knew of two other cases which had not been included in Dr. Weber's list—one that of a gentleman who died a few months ago in Liverpool, the other a man at present under the care of his colleague, Dr. James Barr, in the Liverpool Royal Infirmary. In fact, no less than six cases in all had come more or less under his own observation during the last five years. His view that the condition of myelopathic albumosuria was a definite morbid entity was clearly shared by Dr. Weber, and was, he believed, now generally accepted. After congratulating Dr. Weber on his paper, he referred to the well-marked case of this disease at present in the Liverpool Royal Infirmary. "The patient is a man aged forty-eight, who has always enjoyed good health. For some weeks he was in one of the surgical wards, where he was seen by my colleague, Sir William Banks, who recognised that he was the subject of some disease of the vertebrae, and an examination of the urine at once revealed the true nature of the affection. About ten days ago he felt as if something gave way in his back; paraplegia came on quite suddenly, and has been followed by cystitis, and no doubt the end is not far off." As regards the question whether this peculiar proteid ought to be denominated an albumose or an albumin, it must be admitted that custom seemed to have decided in favour of calling it an albumose, and scientific grounds for thus classifying it were not altogether wanting. In its chemical behaviour it seemed to be in a sense

intermediate between true native albumen and proto-albumose. The coagulum by heat was much more soluble than that obtained from native albumen, and had been said not to be a true heat-coagulum at all, while the nitric acid reaction was identical with that of proto-albumose. On the other hand it was not dialysable. The term albumose was applied by physiological chemists to bodies which differed considerably from one another in their chemical reactions. Thus one member of the group, hetero-albumose, was insoluble in distilled water; proto-albumose was coagulated by  $\text{HNO}_3$ ; deuterio-albumose was not so. The essential idea of an albumose was a proteid derived from albumen, but with a smaller molecular weight and of less complexity than the latter. As far as was known, all the albumins commonly met with contained, among others, a hetero-albumose group or radicle, and yielded hetero-albumose and other albumoses when digested. But Magnus-Levy declared that Bence-Jones proteid did not contain the hetero-albumose complex, which appeared to be the same as admitting that it was a proteid, obviously derived from albumen, but of less complexity, and presumably with a smaller molecule than the latter. If this were so the Bence-Jones proteid came within his (the speaker's) definition of an albumose. The clinical picture of the disease was now practically complete, the diagnosis absolutely clear, and the prognosis, unhappily, absolutely certain. It might be considered as settled that the new growth in the bones was the seat of the formation of the albumose. In regard to the aetiology of the disease, little or nothing definite was known except that it showed a marked preference for the male sex. The question whether it might have some relation to antecedent syphilis had not received the attention it deserved. Its greater incidence in the male might be held to suggest some such relationship. Of the four cases in which he had had an opportunity of investigating this point, one was actually suffering from tertiary symptoms, though the patient denied that he had ever been infected, and another gave a distinct history of venereal infection. In spite of the histological conditions found, he considered that this was not a disease of the same class as ordinary malignant sarcoma. Whether that gave ground for the hope that the disease might at some time be found amenable to treatment he was not prepared to say, but it was a notable fact that in at least one instance the existence of albumosuria had been detected eight years before the fatal termination.

Dr. R. HUTCHISON, speaking from the chemical point of view, said that the chief point was to determine where this large amount of proteid present in the urine was produced. After an examination of all the organs, an identical proteid was not found in any of the organs, and one only somewhat like it was found in the portion of new growth alone which replaced the bone-

marrow. This seemed the most likely source, and it raised the question whether the curious granules seen in the sections were not this proteid, and whether they might not be compared with the granules of eosinophile cells.

Dr. J. J. R. MACLEOD said, with regard to the exact chemical nature of Bence-Jones albumose, that its chemical reactions would indicate that it belonged to the native proteid group rather than to the proteoses. The biuret reaction was of a distinct violet colour, not the rose-pink which was characteristic of the proteoses. From its other reactions no definite opinion could be deduced. To decide whether the albumose proteid was derived from the gastro-intestinal tract or not, it would be necessary to restrict the proteids of the diet to a greater extent than had been done in Dr. Weber's case. By its chemical reactions its chemical nature could not be determined, but this in any future case might easily be done by injecting it into the blood of an animal and finding if a specific precipitin was developed.

Dr. W. LEE DICKINSON thought that Dr. Weber had established two points,—that the condition occurred mainly, if not exclusively, in tumours of the bones, and that the substance was probably produced in the bone-marrow. The absence of the substance in osteomalacia and fragilitas ossium was remarkable, as also in lymphadenoma of the bones; cases of these diseases were quoted. He asked if there was excessive excretion of lime in Dr. Weber's case. Albumosuria was occasionally associated with diabetes, a disease in which, like osteomalacia, there was sometimes excessive excretion of lime.

Dr. HUTCHISON said he had not estimated the amount of lime present, but the proportion of the earthy to the other phosphates was unusually high.

Dr. WEBER, in reply, said that it was to be hoped that in every case of metastatic implication of the bones the urine would be examined for the Bence-Jones proteid. The diet test he had carried out was not quite satisfactory, but it was of value in that a considerable dietetic change had been made which resulted in no alteration in the amount of Bence-Jones proteid in the urine. The cases of Bence-Jones albumosuria could hardly at present be considered to be precisely identical with each other. In one undoubted case of lymphatic leukæmia Bence-Jones proteid was found in the urine, but in the case in question the bone-marrow might conceivably have been the site both of leukæmic growth and of growth like that in Dr. Weber's present case.

# CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS

AND ITS

TREATMENT BY PYLOROPLASTY

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THE main points that we desire to put forward in this paper are (1) that congenital hypertrophy of the pylorus is probably a far more frequent affection than is supposed; (2) that the condition is still not generally recognised, for the symptoms may easily be misinterpreted or overlooked; and (3) that the affection may be successfully treated by pyloroplasty. In support of the last proposition we furnish two illustrative cases.

The condition that has been described principally under

the cumbrous title of "congenital hypertrophic stenosis of the pylorus," or of "congenital gastric spasm" (94), among other names, has really only been recognised for a very few years; and the literature of the subject, though tolerably voluminous, is confined to scattered pamphlets, papers, and brief reports. Most of the text-books and standard works make no mention of the condition whatever, while a few refer very briefly to it.

Specimens of the condition are not commonly found in museums.<sup>1</sup> It by no means follows that the condition is exceedingly rare. Museum specimens are mostly derived from in-patients in our hospitals, and the symptoms that these infants show lead rather to out-patient treatment. Probably most of those who have experience of out-patient treatment of children in hospitals or dispensaries can recall cases where the condition may have existed and been overlooked. The vomiting is seen only by the parent or nurse, and its peculiar nature may easily pass unnoticed by them. Systematic examination of the abdomen is not invariably made by the medical man in the case of infants seen for troubles of, apparently, an every-day character. In general practice the non-recognition of the condition when it exists is even more likely. This is no imputation of want of care or skill, for continuous close watching is needed to establish the diagnosis.

In a paper (12) read before the Society on November 8th, 1898, a *résumé* of seventeen recorded cases, collected from medical literature, was given, together with details of two fresh cases and of a specimen in St. Bartholomew's Hospital Museum. This gives a total of twenty cases only, although the first record of the affection dates back at least to 1788.<sup>2</sup>

Although only five years have elapsed since this paper

<sup>1</sup> The museum of St. George's Hospital contains three specimens; one of these is from Case 17 in Table I.

<sup>2</sup> Williamson (100) is generally credited with the first mention of the condition, but Dr. W. Osler has kindly drawn our attention to a still earlier record, quoted below in the Appendix to the Bibliography.

was written, the total number of cases now recorded is well over fifty. No cases of operation were recorded in this first paper. In the table given below we are able to set forth the details of nineteen cases of operation. Numerous instances of the condition have come under the notice of individual observers. Dr. John Thomson writes that he has met with eight cases in eight years. One of us has seen seven cases in the last five years. Of these seven cases six occurred in the Pimlico district and one at Hampstead.

Reference to the Registrar-General's reports suggests strongly the probability that instances of the affection pass unnoticed. In the statistics of deaths for England and Wales for the years 1891 to 1900 inclusive, under the heading of "Deaths from ill-defined and not specified causes," we find that in the first year of life about 19,000 deaths annually are ascribed to "Debility, Atrophy, and Inanition." Thirteen thousand six hundred odd of these occur in the first three months of life, and about 3300 between the ages of three months and six months.

The subjects of the affection under consideration, if untreated, die at about the third or fourth month. It is not unreasonable to assume that some of the cases in which death is ascribed vaguely to "Debility, Atrophy, and Inanition" are instances of this affection, and it is highly probable that if attention becomes more generally drawn to the condition many more cases will be recognised and, it is to be hoped, successfully treated.

The following is a short summary of the seven cases above referred to, the date and age given being those at the time of death or of operation:

1. May, 1897.—Male aged 14 weeks; death nine days after admission to the hospital. Weight 7 lbs. 4 oz. ('Med.-Chir. Trans.,' 1899, vol. lxxxii).

2. May, 1897.—Male aged 7 weeks; died as an out-patient (loc. cit.).

3. June, 1900.—Female aged 3 months; died on the

day after admission. Weight 6 lbs. 3 oz. ('Lancet,' 1900, vol. ii, 256).

4. February, 1901.—Male aged 9 weeks was under treatment as an out-patient, and was admitted into hospital under a colleague. Weight 4 lbs. 6 oz. two days before death; was said to have weighed 8 lbs. at birth (Blackadder, 'Brit. Med. Journ.,' 1901, vol. i, 765).

5. March, 1902.—Male aged 2 months; examined post mortem. Was under the care of Dr. Champneys, who has kindly allowed us to make mention of the case ('Brit. Med. Journ.,' 1902, vol. i, 1340).

6. June, 1902.—Male aged 8 weeks (*vide infra*).

7. August, 1902.—Male aged 6 weeks (*vide infra*).

All these cases were typical instances of the affection. The undue preponderance of males in this series is unimportant, for the larger series of collected cases shows that females are almost as often affected.

One noteworthy fact is that a fatal issue results before the fourth month of life in infants not operated upon.

The two fresh cases need be only briefly recorded. They are as follows:

CASE 6.—Boy, H—, was born on April 14th, 1902, and was described as "a lovely fat child." He was the fifth child of a mother aged thirty-nine, who had had no miscarriages and had no difficulty in rearing her other children. For six weeks he was fed on condensed milk, and for one week on diluted cow's milk.

Vomiting began at the age of three weeks, and persisted. The bowels were described as costive and as acting about once a day.

On May 31st, at the age of seven weeks, he was admitted into the Belgrave Hospital for Children, having been vomiting continuously for two days. He was very wasted, weighing 8 lbs. The tongue was clean, and the fontanelle was depressed.

June 4th.—Has vomited daily. Several feeds might be kept down, and then a large quantity of curdled milk was



brought up at once. A small amount of dry brown faecal matter was passed daily. Loss of 5 oz. in weight. Dilatation of the stomach and visible peristalsis were readily made out.

June 9th.—The vomiting has been more frequent. Loss of 4 oz. in weight.

10th.—Pyloroplasty by Mr. Dent. The details of the operation will be described later in this paper. No food was injected into the intestine during the operation.

*Feeding after the operation.*—He was immediately given a rectal feed of two ounces of peptonised milk and water, equal parts, and a few drops of brandy. These feeds were repeated every three hours day and night for six days, and the bowel was washed out once a day with saline solution. The injections were then not retained so well, and were given less often, being finally omitted in another two days. By the mouth a teaspoonful of hot water was given every quarter of an hour for thirty hours. Then he received a like quantity of whey, the amount being doubled forty-eight hours later. On June 17th he was fed on peptonised milk and water, and on June 23rd he began to take diluted cow's milk.

The vomiting continued after the operation, but altered in character. At first the bulk of the hot water was returned. Twelve hours after the operation some altered blood was brought up. A week later the vomiting ceased, but up to the time of discharge he occasionally was a little sick.

About thirty-six hours after the operation faecal matter and altered blood were passed *per anum*.

*Complications.*—Edema of the feet began on June 15th, and next day appeared in the face. It persisted for a week, and was associated with a slight degree of albuminuria. It was probably due to a mild attack of desquamative nephritis from too much work being suddenly thrown upon the kidneys.

The wound also gave way at the lower part. The edges of the wound were dry, and in the child's debilitated condition showed at first little tendency to heal. No

doubt the anterior wall of the stomach became adherent over a small area to the abdominal wall on either side of the lower part of the wound.

*Weight.*—Eight days after the operation the child weighed exactly a pound more than he did the day before the operation. Some of the gain was due to oedema.

On June 29th the wound had quite healed, and a week later the child was discharged in fairly good condition, but he did not assimilate his food well, and actually weighed on discharge an ounce less than on admission. The food passed readily through the pylorus, and he took it eagerly and without vomiting. It was hoped that fresh air would stimulate his assimilative functions.

*Subsequent history.*—He was re-admitted on July 29th for an attack of diarrhoea due to unsuitable food. His weight was 9 oz. more than on his discharge. For nearly three weeks his stools were not satisfactory, and his weight kept almost stationary. On August 16th he weighed 8 lbs. 10 oz., and he then started improving, until on September 3rd he had reached 9 lbs. 10 oz. in weight, and looked well and happy. He was sent out daily in charge of a sister, and from some unexplained cause he unfortunately was seized with an attack of zymotic enteritis, and died on September 9th.

The case may fairly be claimed as one of recovery from the original mischief. The pyloric orifice readily allowed the passage of food through it, and the child was rapidly recovering from the marasmic state into which he had sunk before the operation. At the time the fatal attack began he was rapidly gaining weight, was digesting his food well, and looked like a normal healthy babe.

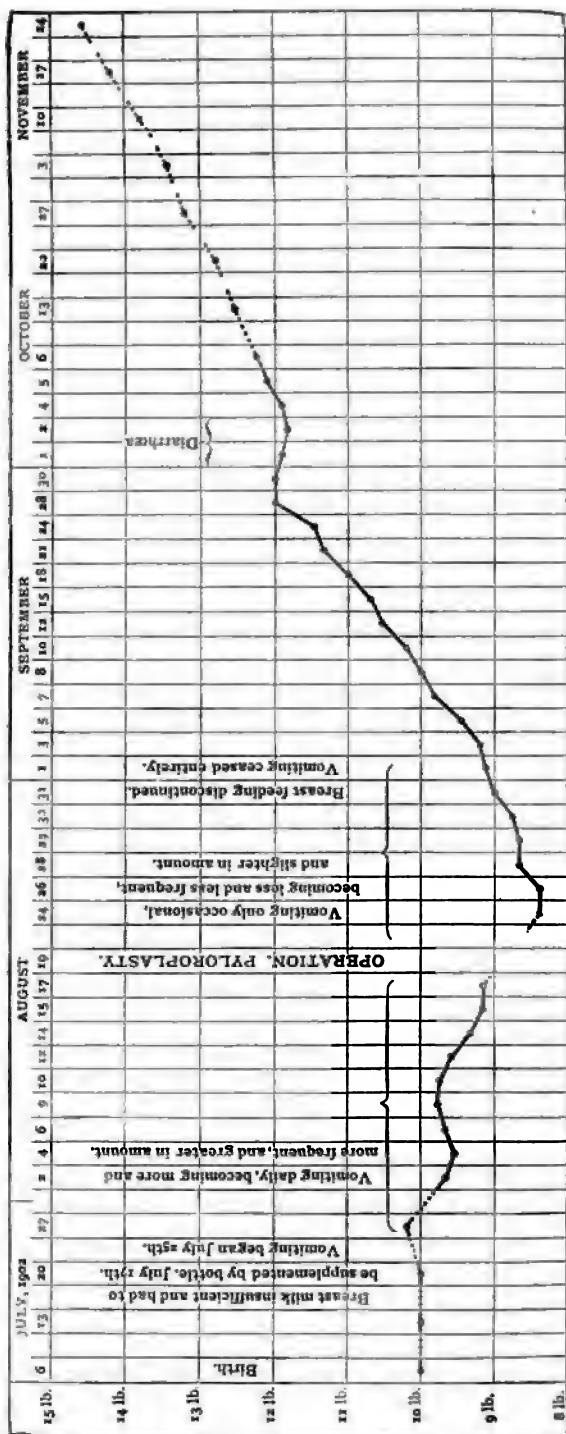
CASE 7.—Boy, M—, was born on July 6th, 1902, and weighed 10 lbs. He is the third child, the two previous boys being strong and well. From the first the mother noticed that he did not take the breast readily like the previous children, and that he was soon satisfied.

On July 27th he weighed 10 lbs. 6 oz., but he then started severe vomiting, and lost 12 oz. in four days. At first the vomiting was very bad, everything being brought up in from ten minutes to an hour. The stools were variable, and not noticed to be markedly small. During the first ten days of life he was breast-fed, and then for a short period he was partially bottle-fed, on account of pyrexia and a tender breast in the mother.

On August 13th he was seen in consultation with Dr. James Morrison, who had recognised the presence of some obstruction. The child looked ill, the eyes were sunken, the tongue clean, the weight 9 lbs. 6 oz. The stomach was dilated, and peristaltic movements could be seen passing onwards to the pylorus, there pausing, and then continuing onward down the duodenum. Deep down under the liver, at the point of temporary pause in the peristaltic wave, could be felt an ill-defined, rounded, movable tumour. The last stool was greenish and contained a little faecal matter. Temporary measures in the way of diet and drugs were tried for a few days, but as the child steadily lost ground and the vomiting was characteristic, pyloroplasty was performed by Mr. Dent on August 19th.

A little altered blood was brought up during the next night. Faecal matter was passed on the third day, and on August 28th the child was gaining weight. During the next four weeks he gained no less than 3 lbs. His recovery was steady and uneventful. The post-operative treatment and feeding were conducted on the same lines as in the other case.

The condition of this child (Case 7), who was in a good station of life, was far better than that of Case 6 at the time of operation. The accompanying weight chart of Case 7 furnishes at a glance a better idea of the clinical history and of the improvement that followed operation than any written description. In this case the previous history and the early symptoms noticed could be thoroughly relied on, as the father was a medical man



and the mother a highly-observant woman. The only *contretemps* during the gestation period were that the mother had at the fourth month trouble with her teeth, some of which had to be stopped, and during the fifth and sixth months her two other children had whooping-cough, which gave rise to some anxiety.

It is worth recording, though we lay no stress on what may be merely a coincidence, that the grandmother on the father's side lost a sister in infancy whose death was ascribed to "nothing passing through her stomach." This child "vomited everything." Nearly all the cases hitherto recorded seem isolated instances.

Cases 6 and 7 seem to be the first in which the operation of pyloroplasty has been adopted for the relief of congenital stenosis of the pylorus in infants. Before discussing the choice of operation a few remarks may be offered on certain points in connection with the affection.

*Diagnosis and symptoms.*—There is little that can be added to what has already been written on these points. The clinical histories in so large a number of the recorded instances so closely resemble each other in every detail that a description of one is typical of all. Cases 6 and 7 are characteristic examples. Once established the symptoms will vary little. The rate of downhill progress is uniform, as evidenced by the steady loss of weight; and, after all, this is what would be expected in a process of death by starvation, the result of mechanical obstruction. Some gastritis may, but only rarely, supervene; dilatation of the stomach is far more likely to ensue, but there are few other changes of moment. If any toxæmia, dependent on the constipation, is brought about, the temperature may be irregular. One word of warning may be given on the question of diagnosis. We must not take for granted that every infant suffering from vomiting and constipation is afflicted with this disease, though these are the main symptoms that attract attention. Such symptoms are, of course, common in infancy. The additional evidence afforded by dilatation of the stomach and the presence of

visible gastric peristalsis is of the utmost value, but an absolute diagnosis can only be arrived at by very careful observation of the symptoms and of the course of the illness. The pyloric tumour, even when of considerable size, may not be perceptible. It will probably lie close to the middle line, and unless an anæsthetic is given for the examination may not easily be felt. The difficulty in deciding the question of operation may be considerable. Some days' observation may be necessary to establish the diagnosis. On the other hand, the earlier the diagnosis is made the greater is the chance of recovery by surgical measures.

*Morbid anatomy.*—The essential abnormality, as all agree, and as the sections show, consists in a marked excess of the muscular fibres encircling the pylorus.<sup>1</sup> There is also some increase of the longitudinal fibres, but, comparatively, to an insignificant extent. This thickening of the circular fibres constitutes merely a hyperplasia, and of itself is sufficient to give rise to all the symptoms. Some authors have found, also, thickening of the submucous tissue (16). Thus Thomson (94) states that "the submucous coat is sometimes greatly thickened, sometimes slightly so, and sometimes it is normal." In neither of our cases was there any thickening of the submucous tissue; indeed, there appeared rather to be atrophy, due to pressure. The mucous coat could be drawn out with great ease. The naked-eye appearance, in transverse section, suggests submucous thickening, especially in spirit preparations, but we do not suggest that those who describe submucous thickening to a greater or less extent have been deceived by the appearances. The term "thickening" of the submucous coat is not a good one, as it would seem to imply that the condition is due to some slow preceding inflammatory process. No writer, however, whether ascribing the stenosis to spasm or hyperplasia,

<sup>1</sup> Finkelstein (28) mentions a case in which the stenosis appeared to be due to increase in the longitudinal fibres. Possibly this appearance was owing to the section not being actually longitudinal.

has suggested that there is any antecedent inflammatory process. Dr. Thomson (94) describes a case which he examined post mortem, in which the "thickening" seems to have been purely an increase in the amount of sub-mucous "lymphoid" tissue. Such a condition would clearly obstruct the passage of the gastric contents through the pylorus. Even though the muscular spasm of the sphincter were relaxed, the loose redundant mucous membrane would impede the flow. Our experience leads us to believe that material thickening or increase in the sub-mucous lymphoid tissue is exceptional in infants. This view is borne out by the sections figured, and by others we have examined. A single longitudinal reduplication of the mucous membrane, much more marked than any other fold, forms a conspicuous feature in many of the specimens. This prominent fold, which resembles the "verumontanum" of the male urethra, is particularly well shown in the specimen figured. Indeed, these stomachs in appearance and feel curiously resemble the dissected-out bladder and prostate, the latter being comparable to the thickened pyloric portion.

*Choice of operation.*—It must be premised that the following remarks are intended mainly to apply to the pronounced cases of the affection, where operation seems indicated in the first few weeks of life.

Various operations have been performed for the relief of the condition. As far as we have been able to ascertain from the records of published and unpublished cases, operation has been performed in nineteen instances. These are set out in Table I. The average age at which operation was performed in the first eighteen cases was seven weeks.

*Pylorectomy.*—Pylorectomy has been performed on one occasion. This patient, *æt.* 9 weeks, died. There appears to be a general consensus of opinion among those who have written on the subject that pylorectomy is a needlessly severe operation. The fatal objection to it is that the operation must be prolonged, and in the case of abdominal operations on very young children it is essential

to select the most rapid method likely to give good and permanent results. There is little need to elaborate the arguments against this method of surgical treatment, for it is not likely to be adopted again.

*Gastro-enterostomy.*—Gastro-enterostomy has been performed in nine cases. Four of the patients recovered and five died. In one of these patients Murphy's button was used, and death resulted thirty hours after the operation from obstruction caused by the button. The time that is saved by the employment of Murphy's button is more than counterbalanced by the risk attending its use. An obvious objection is that the button, supposing that all goes on well, may drop ultimately into the stomach and not into the intestine. There would be no chance of its passing from the stomach through the stenosed pylorus. Even those who hold that the condition is purely due to spasm of the pylorus would admit the extreme improbability of the pyloric sphincter allowing the passage of so large a body as even the smallest Murphy's button. The argument that has been adduced in favour of using Murphy's button in certain cases of pyloric stenosis in adults, that even if it should drop back into the stomach it can be easily and safely removed by gastrotomy, need hardly be taken seriously. However favourable the operation of gastrotomy be in its results, it can hardly be held justifiable to adopt a proceeding which will probably necessitate this second operation.

While all are of one opinion as to the unsuitability of Murphy's button in these cases, most of those who have written about the affection advocate the operation of gastro-enterostomy.

Weill and Péhu (99), *e. g.*, say that gastro-enterostomy is essentially the operation to be preferred (*la méthode de choix*) from the surgical point of view.

Robson and Moynihan (79) write, "The operation of choice in all such cases is clearly gastro-enterostomy."

Löbker (52) seems to think that gastro-enterostomy is the only operation that can save life, and other writers appear



to hold similar views. Löbker finds his rather positive opinion apparently on two cases, one of which died and one recovered. *Ex cathedra* utterances of the kind do not advance knowledge, and are surely premature when experience of the surgical treatment of the affection is still so limited.

These quotations, by no means all that could be cited to the same effect, show a very decided consensus of opinion. At the same time the number of cases which have actually been submitted to operation is so small that the preference for gastro-enterostomy must clearly be founded on theoretical considerations rather than on actual experience. By some the operation is recommended on the ground that the affection is really one of spasm of the pylorus. If by operation, then, the contents of the stomach can be passed into the small intestine, the pylorus, it is held, is rested, and in process of time the condition may subside and the pylorus resume its proper function. Whether this actually happens or not we do not know at present. The cases that have died have died very shortly after operation, and, so far as we are aware, no opportunity has yet occurred of examining post mortem any case in which gastro-enterostomy had been performed for this condition some time previously. It must be remembered that it is only within the last three or four years that any of these cases have been submitted to operation. To this point we revert later on.

Writers who do not hold that the condition is essentially due to spasm in all instances equally favour the operation of gastro-enterostomy, believing it to be one that fully meets the requirements of the case. Now, we are not concerned to deny the fact that gastro-enterostomy may bring about effectually the relief of all the symptoms. As some of the cases cited in Table I show, the vomiting ceases, the bowels act properly, and the child begins to gain weight. In short, life is saved and health is restored.

Our contention is that a similar result may be obtained by means of pyloroplasty, and that this operation is, on

surgical grounds, to be preferred. It would be unwise to draw any large deduction from a small number of cases, but it may be pointed out that of the nine cases in which gastro-enterostomy was performed more than half died.

The objections to our mind to the choice of gastro-enterostomy are—

(1) That it necessitates a considerable exposure of the abdominal contents.

(2) That the operation must necessarily be more protracted than either dilatation of the pylorus or pyloroplasty. All will agree probably that the gastro-enterostomy should be done by simple suture. In the case of a very young child the parts are so small that the delicate manipulation required by the operation, if efficiently performed, must take considerable time. The use of very minute Senn's bone plates, or similar contrivance, would scarcely shorten the proceedings.

(3) That there is increased risk of protrusion of the intestine.

(4) That the incision has to be prolonged further down towards the umbilicus. Wounds in the epigastric region, as is well known, heal most readily, and the resulting scar is strong, without any tendency to subsequent ventral hernia. In a little child the upper part of the abdominal wall is probably further developed and the ventral plates are more closely approximated than lower down in the belly.

So far as we have been able to ascertain, anterior gastro-enterostomy has been adopted in all the cases operated on. Posterior gastro-enterostomy, the better operation of the two, is open still more markedly, in the case of an infant, to the objections already urged.

To our minds the operations of dilatation of the pylorus and pyloroplasty are both superior to gastro-enterostomy for these cases, and there is really not much choice between the two methods. Both can be done through a very small abdominal incision, which is situated high up in the epigastric region; both can be done in a short time and without even seeing any of the intestine, and therefore

with the minimum of risk of protrusion of the abdominal contents. Both operations again—as the cases cited in the table show—can bring about quite as complete recovery as the operation of gastro-enterostomy.

It would probably be hardly fair in dealing with so small a number of cases to lay any stress on the fact that more recoveries have followed when these operations have been selected than when gastro-enterostomy has been performed.

Table I shows that dilatation of the pylorus (some form of Loreta's operation) has been performed in six cases; five of these recovered and did well after. One died.

Pyloroplasty alone was performed in the two cases on which this paper is founded, and in a recent case (No. 19). Here, again, the child recovered from the operation, but the case is still incomplete.<sup>1</sup> The case of Sonnenburg<sup>2</sup> has often been quoted. He performed pyloroplasty for the relief of a condition of the kind, but finding that the subsequent result, as regards nutrition, was unsatisfactory, later on performed gastro-enterostomy. After this second operation the patient improved. But this was in a child of six years of age. In our paper we are dealing only with the condition as it is observed in infants, and we therefore have not included this case in Table I. At the same time we fully allow that the case supports the views of those who favour the operation of gastro-enterostomy.

The operation of pyloroplasty has been condemned by several of those who have written on the subject, as it appears to us, on altogether insufficient grounds.

Monnier (60) describes pyloroplasty off-hand as unsafe and often impracticable, on account of the thickness of the pyloric wall.

Robson and Moynihan (79) say, "Pyloroplasty, on account of the great thickness of the pylorus and its rigidity in the whole circumference, is inapplicable." These authors make

<sup>1</sup> This case recovered, and was doing well in May, 1903.

<sup>2</sup> See Table II.

no reference to the operation of dilating the pylorus for this affection.

Weill and Péhu (99) adopt the view of Abel (1) that pyloroplasty is out of the question on account of the induration of the myomatous tissue that constitutes the muscular hypertrophy.<sup>1</sup> Other authors also consider that the operation of pyloroplasty is inapplicable.

The only authors who favour the Loreta method would appear to be Schmidt (82, 83) and Thomson (93).

To sum up, then, it would appear (1) that the balance of opinion is decidedly in favour of gastro-enterostomy, on the ground that recovery follows, and that the operation meets the necessities of the case; and (2) that pyloroplasty is not so much an unsuitable as an impracticable operation.

Now this latter opinion is one that our cases seem clearly to disprove. Notwithstanding the extreme rigidity and thickness of the hypertrophied pyloric sphincter, no difficulty whatever was found in our cases in sewing up the wound transversely. Indeed, the operation of pyloroplasty would be worthless and impracticable in almost all cases if rigidity and thickness of the wall constituted an insuperable obstacle to its performance. It would be extremely easy, of course, to perform pyloroplasty on a healthy normal stomach, but the operation is not called for in such cases. The operation is really very much easier when the thickness is due to muscular hypertrophy, as in congenital pyloric stenosis, than when the pyloric region is thickened, tough, and fibrous owing to inflammatory changes. In very young children it will be found that the stomach and duodenal walls can be approximated with exceedingly little tension, and with no tendency whatever of the stitches to cut through.

A brief description of the operation performed in our two cases will best serve to explain the purely surgical grounds that we have for advocating pyloroplasty.

<sup>1</sup> Loc. cit., p. 1102. "On ne peut y songer en raison de la dureté particulière du tissu myomateux qui constitue l'hypertrophie musculaire."

We may premise that, whatever operation be chosen, a condition for success of the very first importance is the administration of the anæsthetic. It would be difficult to imagine a class of cases in which more depends on the skill and judgment of the anæsthetist. Unless the patient is deeply under the influence of chloroform (which certainly appears to be the best anæsthetic) there is risk of protrusion of the intestine, and rapidity of operating becomes a matter of great difficulty. On the other hand, in abdominal operations on very young children, deep anæsthesia, unless most carefully induced and maintained, may lead to very sudden and alarming symptoms. Any interruption to the operative procedure while in progress would be a very serious matter, for if the patient is not deeply anæsthetised there is every likelihood of his recovering sufficiently to cry or struggle. If any such event happens the intestines are likely to protrude at once with the most astonishing suddenness and force. In Stern's (90) case both of these troubles seem to have occurred. The child's breathing stopped just after the operation had begun; the anæsthetic was so badly borne that it had to be discontinued while the operation was completed; and the result was that the intestine protruded extensively, thus prolonging the operation and enormously increasing its severity. Distended intestines, when protruded in a crying child, are not easily replaced without force. The chief trouble in this case lay in what Stern terms the "*Repositionsschwierigkeiten*." The patient died an hour or two after operation was concluded. The success of our cases was largely due to the extreme care and skill with which the anæsthetic was administered in the first case by Dr. Menzies, and in the second by Mr. Shuter. The surgeon is too often inclined to absorb all the credit of a successful operation, when a great part of it is really due to the anæsthetist.

If there be from any reason difficulty with regard to the anæsthesia, the operation that can be most rapidly

performed and with the least incision is clearly the best to adopt.

In our first case the abdominal wall was so exceedingly thin, and the child so emaciated, that as soon as the fibres of the rectus were separated the peritoneum almost burst open. There is no need to drag the pylorus up into view. If the distended stomach that presents be gently pressed back into the left flank the pylorus will almost immediately rise up into the wound without any traction. The feel and the appearance in these cases is very characteristic, and in both of our cases this portion of the stomach looked paler than natural. The peristalsis and distension excited by the exposure and the handling may be embarrassing, but the moment that the incision is made into the stomach the distension subsides, and the rest of the operation is easy enough. The incision should divide freely the thickened tissues and extend well into normal structure on each side. An inch is really rather a short incision. Even in a very young child no difficulty will be found in uniting the wound transversely with an incision fully an inch and a half in length.

In our second case some of the stomach contents, consisting of undigested and frothy milk, escaped, but was easily prevented from getting into the peritoneal cavity. It was not thought wise to prolong the operation by washing out the stomach. At the upper and lower angles of the wound the mucous membrane was united to the coats of the stomach and the duodenum respectively. As the muscular wall retracts it slides back over the mucous membrane, causing the latter layer to project. There was a marked absence of any submucous thickening, and the mucous coat could have been drawn out with the greatest ease. The object of the two sutures mentioned was to prevent the cut mucous coat from crumpling up unduly, and so creating obstruction when the pyloroplasty was completed.

The widest part of the wound was united first, and this could be done without the slightest injurious traction.

It matters little whether one or more of the sutures penetrate through the whole of the coats or not. If it be desired to examine the inner mucous surface the lateral parts of the wound can be widely separated, and, if need be, the longitudinal fold of redundant mucous membrane, which is likely to be in the line of the greater curvature, can be excised. The introduction and closure of the first suture at the widest part of the wound is likely to so approximate the whole of the wound transversely that there is little trouble from escape of the stomach contents. There is no need to put in many sutures; five or six for an incision an inch and a quarter in length are quite sufficient, and the whole of the serous surfaces can be most effectively and safely apposed with this number. The multiplication of sutures is unwise, for it takes time, and may bring about by necrosis of the tissues subsequently the very leakage that it is supposed to prevent.

No difficulty was found in either case in bringing the serous surfaces at the extreme angles of the transverse wound together in a perfectly satisfactory manner, *i. e.* the parts where the thickening and the toughness of the tissues were greatest were almost as easily sewn together as the central normal parts of the wound. The objection that has been taken to the operation on this ground, therefore, seems to us to be entirely disproved by practical experience.

If any embarrassment arises from the distended intestine, probably the transverse colon, bulging up towards the wound, it can be controlled effectively by the simple device of irrigating with hot normal saline solution. This method is of the greatest value in all abdominal operations in children. Not only are the exposed parts kept warm, but it will be found also that the distension subsides, the intestine, becoming heavy, sinks back into the cavity of the abdomen, while the serous surfaces are kept moist, which is a consideration of the highest importance. The suture of the abdominal wound, too, is rendered easier. Moreover the absorption of the fluid is of the greatest

benefit to the child, for the thirst that so frequently constitutes a great source of distress after abdominal operations is greatly lessened. The fluid contents of the stomach show that the vessels have obviously been unable to absorb the watery constituents properly for some time. The emaciation is largely due to the drying of the tissues.

The operation in the second case occupied just twenty-three minutes, and a good deal of this time was taken up in suturing the abdominal wound. The time during which there was really any exposure of the abdominal contents was therefore very short.

A practical point in the after-treatment consists in keeping the child on its right side as much as possible. This plan certainly seems to facilitate the passage of the stomach contents on into the duodenum.

It was very noticeable in both operations that there was no transverse gaping of the wound when the incision was made through the sphincter. Yet this might have been expected if the muscle was in a state of spasmodic contraction. The cut surfaces, too, of the sphincter remained flat and not concave, as would have happened if the cut sphincter had retracted. The wound did appear to extend longitudinally to a slight extent, owing of course to muscular action.

We believe that pyloroplasty is in these cases preferable to dilatation for the following reasons :

1. It can be done at least as quickly. It has been recommended in Loreta's operation to perform the actual dilatation deliberately. In both operations an incision has to be made into the stomach, and sewn up again.
2. It is a more definite proceeding, and allows more range, as the length of incision can be graduated according to the condition found.
3. The lumen of the tube can be examined, and, if thought desirable, the longitudinal fold of mucous membrane can be removed. This fold will probably, if present, be found in a line with the greater curvature of the stomach.



4. The exact amount of injury done to the parts is known.

There seems to be no advantage in performing what has been termed "submucous pyloroplasty." If there were any distension of the stomach this would be an embarrassing proceeding. It is better to divide all the coats.

*Etiology.*—The causation of the condition is still quite uncertain. Some hold that the condition is due to a primary hyperplasia of the muscular tissue, an overgrowth due to a fault in development. Others consider that the hypertrophy is secondary, and results from over-exertion of the muscle, this being due to functional disturbance of the nervous mechanism of the stomach and pylorus. Dr. Rolleston (75) writes, "It seems reasonable to combine these views so far as to believe that there is some congenital hyperplasia of the pyloric sphincter, and that spasm supervenes on this, and is largely responsible for the symptoms manifested."

Although we do not profess to be able to make any material contribution to solving a question that is still in the nebulous regions of hypothesis, we submit a few considerations on the subject. The discussion of the causation is not a mere academic question. If the condition be due to pyloric spasm, as Pfaundler (70) maintains, in all cases, the affection should be amenable to treatment short of operation; and the fact that medical treatment in marked cases has hitherto proved futile should not deter us from seeking for more efficient remedies than have hitherto been found.

As in our view the condition is more probably due to a muscular hypertrophy which is not the result of spasm, we hold that while surgical measures are imperatively demanded in the strongly marked cases, they may also be with advantage adopted even in slight degrees of the affection. Undue delay, especially in cases that are not of the severest type, is likely to lead to dilatation of the stomach; and when the stomach is much dilated the results

of operation of any kind are far less likely to be good. The food may be able to get out of the stomach, but it will not be properly assimilated.

Dr. Thomson (95), in a recent paper, argues fully and with much ingenuity in favour of the hyperplasia being secondary to spasm. The argument in support of the contention that the hyperplasia of the muscle is secondary may be summed up briefly as follows:—The stomach is not an inactive organ during intra-uterine life, but its contents—mainly the liquor amnii—pass through it on into the intestine. As a result, presumably, of derangement of the nervous mechanism there is inco-ordination; even slight disturbance of co-ordination may lead to greatly exaggerated exertion. If the inco-ordination is of a violent spasmodic kind, it must inevitably result in great muscular hypertrophy. This theory seeks to explain, therefore, the congenital muscular hypertrophy as a result of muscular spasm commencing in intra-uterine life.

In support of the opinion that the muscular hypertrophy is due to over-action, it is urged that no other isolated deformity, or abnormality of the same nature, is met with as a congenital defect.<sup>1</sup>

The excessive growth of the muscular tissue of the uterus which takes place during pregnancy is alluded to, but dismissed at once as a thing altogether by itself.

With regard to local giantism, such as is often seen of a digit, or of the tongue, it is argued that such abnormalities are not parallel cases. A local giantism of the pylorus might be possible, but hardly a primary true hypertrophy of a muscle, which forms only a portion of the pyloric structure.

The weak point of the argument to our mind lies in the

<sup>1</sup> Possibly the sublingual fibromata of the newly-born that have been described by Italian surgeons may furnish a parallel case. These little tumours appear to be a purely local hyperplasia and hypertrophy of the mucous membrane. 'Jahrbuch für Kinderheilk.,' Band i, Heft 5, 1900, S. 532. Callari and Philippson, "Ueber das sublinguale Fibrome der Säuglinge."

assumption that the muscular spasm is necessarily of so pronounced and prolonged a character as inevitably to lead to hypertrophy.

Dr. Thomson quotes John Hunter as pointing out that hypertrophy from repeated forcible contraction is a property common to all muscles and greater in involuntary than in voluntary muscles. This much may be granted at once, but the proof that any such repeated forcible contraction of the pyloric sphincter takes place, even after birth, in these cases is very far from complete. A pyloric sphincter, though exceedingly small and weak, might effectually close the orifice merely by non-relaxation at the proper time. The muscular fibres of the stomach that drive on the gastric contents into the duodenum do not act in a manner directly antagonistic to the sphincter, and there is no need therefore to assume that any excessive action of the sphincter is necessary to occlude the passage. Hypertrophy of the detrusor fibres, as would be expected, does occur after a time, but the efforts of these fibres to overcome the obstruction would lead rather to pouching of the stomach at the pyloric ring—a condition that is met with in adults—than hypertrophy of the sphincter, for the latter muscle, acting at an immense mechanical advantage, is not a direct opponent to the longitudinal and oblique muscular bands.

In answer to the challenge to cite any other instance of a local giantism or hyperplasia of a sphincter muscle such as that of the pylorus, it may fairly be asked what other instance can be given of a sphincter muscle becoming hypertrophied to the same extent as a result of spasmodic action. The very term implies intermittent action. No such hypertrophy is seen in the case of the anal sphincter, or in that of the bladder, or of the cardiac end of the stomach. But in the first two the tonic contraction is more constant.

It has been urged that in the subjects of congenital hypertrophic stenosis the pyloric sphincter increases greatly during the first few weeks after birth. Still remarks that

the pylorus cannot be felt until the fourth week. The capacity of the stomach increases rapidly during the first few weeks after birth. Observers agree that the capacity of the stomach is about two and a half times as great at the fourth week as in the first week.<sup>1</sup> The muscular tissue also, with increased functional activity, becomes more evident. The organ, therefore, would, as a whole, be more recognisable by the fourth week of life. But an enlarged pylorus could be detected earlier, though perhaps not clearly made out without an anæsthetic. Inasmuch as cases of congenital pyloric stenosis are uncommon, and the condition is rarely, in the absence of symptoms, suspected for the first two or three weeks, the tumour is not found because it is not looked for. As the child emaciates the detection of the tumour becomes easier, but this is no evidence of any rapid increase of the pyloric tumour. The more widely the affection becomes known the earlier will the pyloric thickening be detected.

The discussion of the possibility of this congenital affection persisting and giving rise to trouble first noticed later in life hardly falls within the scope of this paper. Cases such as those of Sonnenburg (in a child aged six), of Hansy (in a boy of eleven), among others, suggest the possibility (see Table II). We are permitted to mention also the case of a girl aged twenty-two, recently under the care of Dr. Rankin and Mr. Pendlebury, who had suffered from periodic attacks of vomiting for sixteen years. There was pyloric trouble, possibly congenital, indicative of arrested development.<sup>2</sup>

In cases of the like nature there is no prodigious mus-

<sup>1</sup> Cf 'Traité des Maladies de l'Enfance,' tome deuxième, "Maladies du tube digestif: Considérations pratiques sur le développement physiologique du tube digestif chez l'enfant," par G. Variot, p. 296, 1897.

<sup>2</sup> There is a specimen (Series IX, 422) in St. George's Hospital Museum showing pyloric stenosis in a man aged 56. There is a great excess of muscular tissue similar to that observed in the congenital form, and possibly this is an instance of persistence of the condition. There appears to be no malignancy whatever.

cular development of the sphincter such as the hypothesis of muscular spasm would seem to demand. There is more likely to be fibrous thickening due to interstitial changes. Of such interstitial changes there is no trace in the infantile form.

Our knowledge of the nervous mechanism of the stomach is, as yet, so imperfect that it seems premature to found any hypothesis as to the causation on a theory of lack of co-ordination.<sup>1</sup>

The results of operative treatment throw but little light on the question. The success that has attended the various surgical measures is consistent with any of the explanations of the causation hitherto advanced. Forcible dilatation of the pylorus or pyloroplasty would overcome spasm or would restore the lumen of a passage that had been compressed by an excessive muscular development. At first sight it would seem natural to suppose that after a time the muscle would recover, and that the spasm would return, and this might be held to favour the view that pyloric spasm is not the real factor. The sphincter ani, for example, recovers its power after forcible stretching. We can hardly imagine that forcible dilatation could bring about proper co-ordination, which depends on the innervation of the gastric muscles. Practically, the mechanical obstruction is relieved by the mechanical stretching or, even more efficiently, by pyloroplasty. Though it is premature at present to say that recovery is permanent, as far as experience goes the good effects may at least be prolonged for months or years. The fact that gastro-enterostomy may bring about recovery from all the

<sup>1</sup> Among the most recent views on the innervation of the stomach and pylorus are those of Openchowski, who states: "*Pylorus and antrum*.—Central centres which cause constriction lie in the corpora quadrigemina; the fibres run almost entirely in the vagi. In the corpora quadrigemina are also centres for causing the pyloric sphincter to gape; apparently the path is down the cord and by the splanchnic nerves. It is of importance to know that the opening of the cardiac end in point of time coincides with contraction of the pylorus." Quoted by Tiegersleddt, '*Physiologie der Menschen*,' vol. i, p. 269, 1897.

symptoms may be held to favour the theory of spasm. 1) Possibly the pyloric sphincter after this operation may revert gradually to its normal extent and functional efficiency, but there is no evidence as yet that it does so. After a successful gastro-enterostomy for a non-malignant condition of the pylorus, the nutrition may become perfectly normal though the pyloric passage remains closed, and this benefit is even more likely to come about in a child than an adult.

On the whole, we are disposed to think that the balance of evidence is in favour of the hyperplasia being primary. The solution of the problem probably lies in the hands of the morphologist. Very little is known about the development of the upper part of the alimentary canal that lies in the abdominal cavity.

The thickness of the normal pyloric sphincter, as the sections show, varies greatly. The specimens are all prepared from the stomachs of children less than twelve months old. Our best thanks are due to Dr. W. J. Fenton for preparing the specimens, and to Dr. H. R. D. Spitta for the excellent micro-photographs made from them; also to others, especially to Dr. Thomson, for information about cases hitherto unpublished.

TABLE I.

No.	Operation.	Age.	Operator.	Result.		Remarks.	Reference.
				Death.	Recovery.		
1	Pylorotomy and duodenotomy (Kocher's operation)	63 days	H. J. Stiles	1	—	Thomson's unpublished case; operation March 7th, 1900	Privately communicated.
2	Gastro-enterotomy	Child	W. Meyer	1	—	Adler's case; child in a very debilitated state; died a short time after operation	Footnote to Metzler's paper, New York Med. Record, vol. liv, p. 257.
3	Gastro-enterotomy (anterior)	6 weeks	Fritzsche	—	1	Monnier's case; did well, and five months later nutrition was satisfactory	Deutsche Zeitschr. für Chirurgie, 1901, p. 361.
4	Gastro-enterotomy (anterior)	8 weeks	Kehr	—	1	Abel's case; pylorus formed a smooth, round, hard tumour about 3.5 cm. in length, and of the same thickness; claims to be first successful case	Münchn. med. Wochenschr., xlv, p. 46, 1899.
5	Gastro-enterotomy	7 weeks	Löbker	1	—	—	Weill and Péhu, Gaz. des Hôp., Oct. 5th, 1901.
6	Gastro-enterotomy	10 weeks	Löbker	—	1	Child in good condition two years after operation; also claimed as first successful case of gastro-enterostomy (July, 1898)	Verhandl. der Deutsch. Gesellsch. für Chirurg., xix, Berl., 1900, p. 148.
7	Gastro-enterotomy	4 to 5 weeks	Kehr	—	1	—	23ster Congress. Verh. der Deutsch. Gesellsch. für Chirurg., April, 1900, p. 124.
8	Gastro-enterotomy	7 weeks	Stern	1	—	Operation in this case had been unduly delayed; anæsthetic discontinued after first incision; the intestines protruded through the abdominal incision; there was much difficulty in replacing them; though the gastro-enterotomy was completed, the child died an hour or two after	Deutsche med. Wochenschr., Sept. 22nd, 1898, vol., xxiv, p. 601.

TABLE I—continued.

No.	Operation.	Age.	Operator.	Result.		Remarks.	References.
				Death.	Recovery.		
9	Gastro-enterostomy (with Murphy's button)	6 weeks	W. Meyer	1	—	Metzler's case; owing to obstruction from Murphy's button, death in thirty hours	Practitioner, 1899, p. 200; New York Med. Record, vol. liii, p. 709; <i>ibid.</i> , vol. liv, p. 253. Privately communicated.
10	Gastro-jejunostomy	35 days	H. J. Stiles	1	—	Thomson's unpublished case; operation, March 14th, 1900	
11	Loreta's operation	8 weeks	Nicoll	—	1	Claims to be second successful case	
12	Loreta's operation	40 days	H. J. Stiles	—	1	Thomson's case; operation May 10th, 1902; weight, 5 lbs. 13 oz. at time of operation. Oct. 3rd, 1902, patient extremely well and weighed 14 lbs. 8 oz. (unpublished)	Brit. Med. Journ., Sept., 1900, p. 578. Privately communicated. May 8th, 1903, remarkably strong child; weight 22½ lbs.
13	Loreta's operation	25 days	H. J. Stiles	1	—	Thomson's case; operation, March 20th, 1900 (unpublished)	Privately communicated.
14	Loreta's operation	2 months	Schmidt	—	1	Going on well six weeks after operation	Archiv für Klin. Chir., von Langenbeck, lxiii, 1901, p. 977.
15	Loreta's operation	77 days	H. J. Stiles	—	1	Child weighed 5 lbs. 8½ oz. before operation (Aug. 13th, 1902); Oct. 3rd, 1902, weighed 8 lbs. 8½ oz., and was doing well in every way; Thomson's case (unpublished)	Privately communicated. May, 1903, child very well.
16	Loreta's operation	8 weeks	F. F. Burghard	—	1	Still's case (unpublished) Oct., 1902. Doing well May, 1903	Privately communicated.
17	Pyloroplasty	8 weeks	Dent	—	1	Cantley's case; operation June 10th, 1902; death three months after operation, from acute enteritis; cause of death unconnected with the operation; vomiting ceased, child gained some weight, and bowels acted normally	



18	Pyloroplasty	6 weeks	Dent	—	1	Cantley's case; operation Aug. 19th, 1902; rapid recovery without any untoward symptoms; month after operation, gaining weight at the rate of one to two ounces a day	See Chart. June, 1908, exceptionally strong child; weight 24 lbs.
19	Pyloroplasty	4½ months	Murray	—	1	Guthrie's case; operation Oct. 23rd, 1902; stomach much dilated. In good health May, 1903.	Privately communicated; case shown at the Society for the Study of Diseases of Children, Oct., 1902

TABLE II.

The two following cases have been cited as examples of the condition, but we have not included them in our table for reasons already given.

No.	Operation.	Age.	Operator.	Result.		Remarks.	Reference.
				Death.	Recovery.		
1	Gastro-enterostomy	Boy, est. 11	Hansy	—	1	"Doubtless case of congenital muscular hypertrophy of pylorus"	Robson and Moynihan, Diseases of the Stomach and their Surgical Treatment, 1901, p. 44.
2	Pyloroplasty	Child, 6 years	Sonnenburg	—	1	Rosenheim's case; nutrition not being satisfactory, gastro-enterostomy was performed subsequently	Berl. Klin. Wochenschr., xxxvi, p. 32, 1899.

## APPENDIX.

Since the paper was written the following additional case has been published:—Aged 40 days; operator, Lendon; operation, incision and dilatation by extemporised dilators. Left hospital in twenty-four hours. Returned when 11 weeks old (weighing 7 lbs. 13 oz.) with pain and obstruction. Abdomen opened again, but as numerous adhesions were found “any attempt to excise pylorus was abandoned.” Child died twenty-four hours later. Symptoms relieved by the first operation. A well-marked case of the disease. (*‘Australasian Med. Gaz.,’* November, 1902.)

Dr. William Osler, of Baltimore, has kindly drawn our attention to a remarkable case published in a volume entitled ‘Cases and Observations by the Medical Society of New Haven County in the State of Connecticut, New Haven, 1788.’ The title of the paper is “Case of Scirrhus in the Pylorus of an Infant,” by Dr. Hezekiah Beardsley. A brief summary:—From the first week the child had “puking or rejection of milk,” in spite of which it grew, but always remained very emaciated. The child lived to his fifth year. The stomach was unusually large, the coats thickened. “The pylorus was invested with a hard compact substance, or schirrhosity, which so completely obstructed the passage into the duodenum as to admit with the greatest difficulty the finest fluid.” Dr. Osler proposes to have the case copied and published in his ‘Archives of Pediatrics.’

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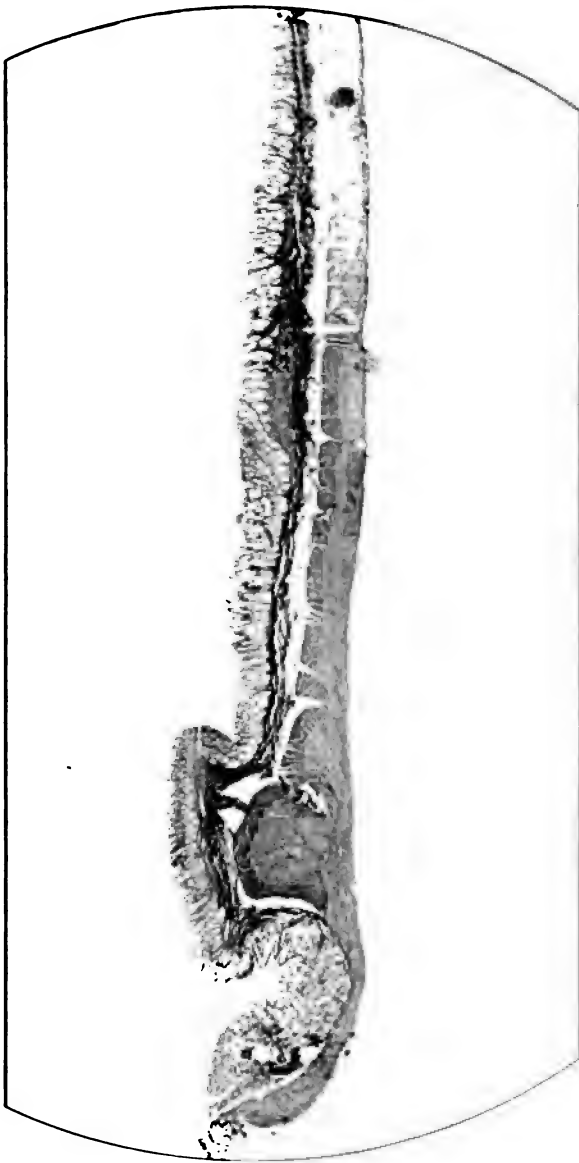




Specimen (natural size) from a child aged 11 weeks, showing a portion of the stomach, the pylorus and commencement of the duodenum in a marked case of congenital hypertrophic stenosis of the pylorus. The pylorus, which has been divided longitudinally, shows excessive thickening of the circular muscular fibres. There is a marked longitudinal fold of the mucous membrane, which, when the cut surfaces of the pylorus are brought together, almost absolutely blocks the opening.



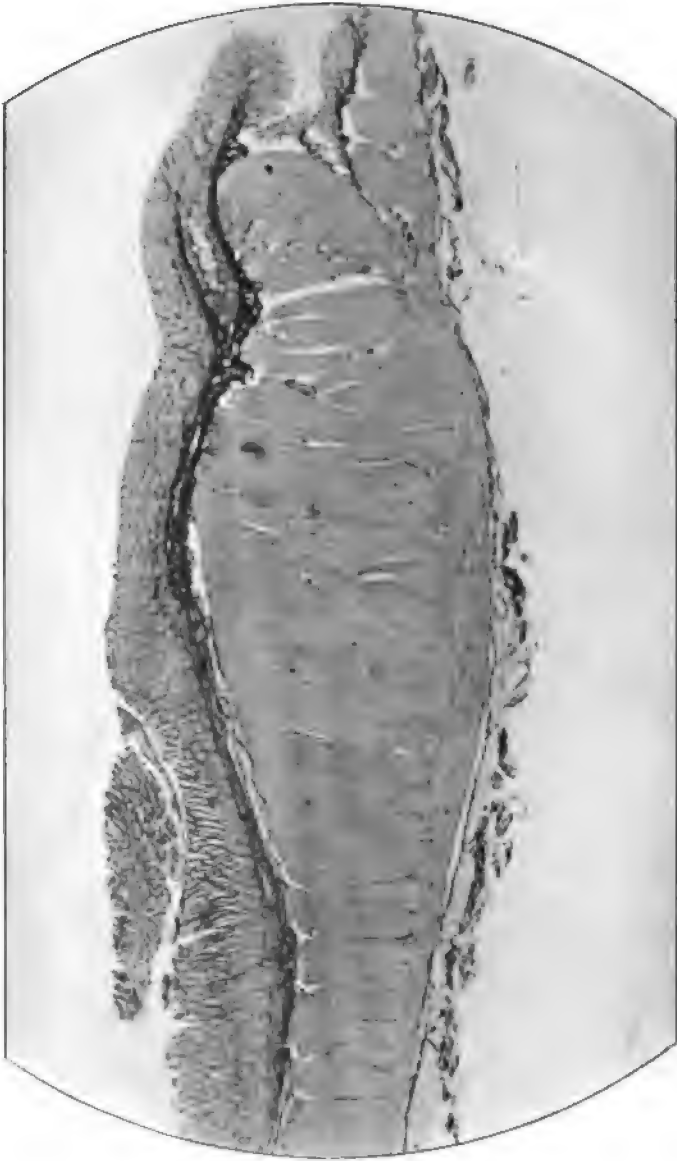
*Cautley & Dent: Stenosis of Pylorus. Plate II.*



Section through the normal pylorus and part of the stomach and duodenum of a child aged 3 months.  
The muscular coat is rather thicker than usual. The sphincter muscle is well-defined. ( $\times 8$ .)



*Cautley & Dent: Stenosis of Pylorus. Plate III.*



Section through the pyloric end of the stomach from a case of congenital hypertrophic stenosis in a child aged 3 months. The thickening of the circular fibres commences some way back from the pylorus. There appears to be a separate pyloric sphincter. The muscular coat at the commencement of the duodenum is also greatly increased in amount. There is very little sut mucous thickening. The specimen has been reversed, so that the duodenum lies on the right. ( $\times 8$ ) Compare with Plate II.



## DISCUSSION

Dr. H. ASHBY (Manchester) said that for many years past he had had a horror of operations on young infants, but recent experience had caused him to change his opinion. The hypothesis which appealed most to him with regard to the ætiology of these cases was that of spasm or abnormal innervation, as against a primary hyperplasia of the circular muscular fibres, or, in other words, a "freak of nature." There was normally a tonic contraction of the circular muscular fibres during the earlier stages of digestion, and a still more vigorous contraction during the act of vomiting. A physiological process might doubtless go wrong before birth just as well as shortly after birth. A disturbance of innervation might produce an abnormal excitation of the circular fibres and an abnormal inhibition of the longitudinal fibres, just as obtained in the case of the heart, or when the flexors overcame the extensors in spastic paralysis of a limb. The evidence went to show that pyloric obstruction from spasm existed in most cases at birth, but that the conditions were made worse and worse by a secondary hypertrophy of the circular fibres at the pylorus, and in some cases there was hypertrophy of the muscular coat at the pyloric end of the stomach, and this in itself rather negatived the theory of a primary hyperplasia of the pylorus. While in some cases vomiting began a day or two after birth, in others there was no vomiting for the first three or four weeks, and it seemed possible that in these the pyloric obstruction might arise from causes in operation after birth. There was certainly evidence that in some cases the pyloric obstruction varied in amount from time to time, and that cases of this nature completely recovered, and recovery would hardly be likely if there were a true hyperplasia from the first. With regard to diagnosis, the typical cases were easily recognised if carefully watched for a few days, especially those who were breast-fed from a healthy mother. It was in these typically severe cases which resisted dietetic treatment that early operation was demanded. In many cases of vomiting in marasmic infants he believed that there was more or less pyloric spasm, and that death occurred before much hypertrophy had taken place. He believed that these were really of the same nature as those described under congenital hypertrophic stenosis, or, at any rate, that there was no marked dividing line between them. That many recoveries took place without operation he had not the least doubt.

Dr. JOHN THOMSON (Edinburgh) agreed with Dr. Cautley and Mr. Dent that the condition was probably very much

commoner than used to be thought. Since February, 1894, he had had eleven cases under his care, in eight of which he had made a post-mortem examination; four of these had died without operation, and four after operation. Two patients had recovered completely after Loreta's operation performed by Mr. Harold J. Stiles, and one was still alive and had not yet been operated upon. He considered that there was a structural change and a functional change in these cases. The essential structural change consisted in true hypertrophy of the muscular coat of the pylorus, stomach, and sometimes the œsophagus. Such other changes found, as narrowing of the lumen of the pylorus and dilatation of the stomach and œsophagus, were to be regarded as secondary. He believed that there was in reality no hypertrophy of the submucous coat, although longitudinal sections of the compressed and puckered mucous membrane might give an appearance of such. The main functional abnormality consisted in a tendency to spasmodic closure of the thickened pylorus, which prevented the normal periodic opening to let through the food. With this there was unduly forcible contraction of the muscular walls of the enlarged stomach. In some cases there seemed to be also at times a spasmodic contraction of the œsophagus. In one of his cases especially this constriction of the gullet was so strong that even a small catheter could only be passed down it with difficulty and pain. There was no symptom characteristic of these cases which might not be regarded with great probability as the result of the excessive ill-timed spasmodic contraction of the hypertrophied muscular apparatus of the pylorus, stomach, and œsophagus. He was convinced that the muscular hypertrophy was merely secondary to over-action. He thought that intermittent muscular over-action was particularly liable to result in muscular overgrowth. That forcible contraction of the pylorus did occur could be verified by palpation of the child's abdomen, when the pylorus could be felt distinctly to harden under the finger. This contraction was certainly not continuous. In the worst cases the pyloric closure might seem to be continuous, so that meal after meal was either vomited entirely or retained unchanged in the stomach long past its usual time. In the less severe cases a good deal of food passed from time to time through the pylorus, and in these much of the fluid passed through while the curd was kept back. After the symptoms had lasted for some time diagnosis could be made with practical certainty, in many cases from the course and character of the vomiting along with such information as could be derived from the use of the stomach-tube. When well-marked peristalsis was recognised the diagnosis became very easy. The important and difficult point to decide, however, was whether the case was bad enough to need operation, or whether there was a reasonable chance of obtaining recovery by the careful use of medical and



dietetic measures. It was certain from the post-mortem experiences of Batten and Hirschsprung, and from the clinical observations of Heubner, Barlow, Still, and others, that some cases of the disease did recover without operation. It was equally certain that many of the cases were quite incurable except by surgical measures. He advocated the advantage of using subcutaneous injections of saline solution in preparing the child to stand the operation as well as after it; and the importance of close personal attention to the minutest details regarding feeding after operation could scarcely be over-estimated.

Mr. HAROLD STILES (Edinburgh) stated that in a considerable surgical experience of this condition the only operation he had not performed was pyloroplasty. He believed that the condition was purely a muscular hypertrophy, not a submucous overgrowth, but whether the muscular hypertrophy was primary or secondary he would not then discuss. The sections which he exhibited, which were taken at various points of the pylorus and stomach, showed that the submucous coat varied considerably in thickness in different places. With regard to the operation which was to be performed, he quite agreed with Dr. Cautley and Mr. Dent that pylorotomy was unjustifiable; he had performed that operation once, and the child had died. The shortness of the first part of the duodenum and the difficulty of attaching it to the stomach were great objections; but it was on other accounts far too severe. He had also done gastro-enterostomy, but the child died on the third day. Of the ten instances of this operation recorded four were anterior, four posterior, and two not stated. Of four posterior two recovered, and of four anterior two recovered. In a third case he had performed Loreta's operation after the method of Dr. Nicol, of Glasgow, using bougies in the first place, followed by dressing forceps to dilate the pylorus; but unfortunately the forceps perforated the posterior wall of the duodenum, and the child died from peritonitis. In two further cases he had performed the same operation successfully, and had found Laborde's tracheal dilator of great service; by means of it the force exerted could be accurately gauged. In one of these cases he had ruptured the anterior wall of the pylorus, but the rent was sutured, and the child made a good recovery. One other case recovered and two others died. Gastro-enterostomy was probably not a good operation. The simplest was the best, given efficiency. He thought Loreta's operation was preferable. It was quicker; there was, moreover, no need to remove the fold of mucous membrane, and the technical difficulties in severe cases were less. Recurrence was not likely to take place after Loreta's operation. Examination of specimens after stretching showed considerable degenerative change in the muscular fibre; thus the spasm and hypertrophy were apparently simultaneously

cured by the stretching, and recurrence of the stenosis was prevented by the atrophy which followed the degeneration of the muscular fibres.

Dr. G. F. STILL said that in addition to three cases which he had recorded in the 'Transactions' of the Pathological Society of London, he had had under his care or had seen in consultation six cases of congenital hypertrophy of the pylorus. He thought that stress should be laid upon the need for very careful consideration before resorting to operative measures in this condition, whether the case be mild or severe. There was now no doubt that complete recovery might occur without operation. Dr. F. E. Batten had recorded one such case, and Dr. Still had seen one typical case in which spontaneous recovery had occurred with careful feeding alone, and another very severe case in which with washing of the stomach, vomiting had now ceased for six weeks, and the child was gaining weight steadily. In another case vomiting had ceased for weeks with similar treatment, but relapse had then occurred and the child died. Even if complete recovery did not occur, an infant was in much better condition for so very serious an operation when a month or two older and several pounds heavier and proportionately stronger. As to the ætiology of this condition, Dr. Still agreed with Dr. Thomson that spasmodic ill-co-ordinated action of the muscles of the stomach and pylorus was the most probable explanation of the hypertrophy; apart from the reasons which had been adduced by other observers he had noticed in at least one case slight thickening of the part of the duodenum immediately below the pylorus, and comparing this with a similar thickening of the part of the ileum just above the ileo-cæcal valve in a case of congenital dilatation of the colon, he suggested that in both cases this seemed most naturally explained by an overflow, so to speak, of spasm. With regard to treatment, he pointed out the difficulty which occurred in the feeding of some of these infants after operation.

Mr. F. F. BURGHARD, in reference to the selection of operation, agreed with Mr. Stiles. In the two cases on which he had operated he had been highly satisfied with Loreta's operation. Gastro-enterostomy and pylorotomy were unsuitable. It was a question of pyloroplasty *versus* Loreta's operation. Loreta's operation could be done more rapidly and with less shock than pyloroplasty when done through a minimum aperture in the abdominal wall, and with a dilator the force of which could be accurately gauged. Hegar's dilators had been very serviceable in his hands, and in each case he had split the peritoneum over the pylorus, and had then stopped. Pyloroplasty seemed to him to be a difficult operation—especially the suturing of the incision in the pylorus. In a recent case he had fed the child on the operating table through a catheter introduced into the duodenum. He had washed out the stomach immediately before the

anæsthetic was begun. The incision should be made high up—starting just over the ensiform cartilage, and coming down only as low as the edge of the liver. He had operated upon two cases, both under the care of Dr. Still, and both had recovered.

Dr. G. NEWTON PITT thought a primary hypertrophy of a portion of a viscus was almost unknown, and local spasms were rare in children, because such are due to some gross or degenerative change. He suggested, too, that there must be some local cause for local spasm to be consistent with the known laws of pathology; such a cause as abnormal stomach contents, abnormal dropping, or kinking of the viscera. There was much in favour of the view that some of the cases recovered. What was the condition of the cases one year after operation? If a local spasm were the cause, the obstruction might well recur.

Dr. H. D. ROLLESTON was reluctant to accept the view that there was primary spasm and secondary hypertrophy. In one case which died after three weeks of life he had seen enormous hypertrophy; this could not have been produced in three weeks. What was the proof that the child normally swallowed liquor amnii? In cases with excessive secretion of hydrochloric acid and spasm of the pylorus, the condition called Reichmann's disease, there was no true hypertrophy of the muscular wall. The idea of primary hyperplasia was, if anything, the less unlikely. The adjacent hypertrophy of the stomach referred to, might indeed be part of the original freak of nature.

Dr. CAUTLEY, in reply, could not accept the primary spasm theory. There was no evidence of spasm or of inco-ordination. No other indication of spasm was observed in these cases. It was not, indeed, an hypertrophy he held, but a hyperplasia. It affected not the longitudinal fibres, but the circular fibres alone, and this was against spasm. Disordered innervation, as of the heart, did not lead to hypertrophy, neither did inco-ordination, as in locomotor ataxia. After intractable vomiting diagnosed as due to pyloric spasm in marasmic infants, no hyperplasia was found *post mortem*—that was, acknowledged spasm did not cause hypertrophy. He testified to the ease and speed of the operation of pyloroplasty. Recovery without operation might occur in the slighter cases. Surgical treatment was indicated in severe cases.

Mr. CLINTON DENT, in reply, reiterated that he did not think there was much to choose between pyloroplasty and Loreta's operation. A main point of the paper was that either operation was a far more suitable proceeding than gastro-enterostomy. He himself preferred to do an operation in which he could see what he was doing, rather than introduce an instrument, and work with an uncertain force. If the cases were at all marked, surgical treatment was imperatively demanded, and if the operation were timely the prospect was favourable. Some children went downhill in spite of all medical measures, and were saved by operation.



# THE OPERATIVE TREATMENT OF GASTRIC AND DUODENAL ULCERS

BY

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IN the following paper I propose to tabulate and to make comment upon a series of cases of gastric and duodenal ulcer, treated surgically, which I have had under my care.

Operative treatment may be required in *perforation* of a gastric or duodenal ulcer, in *hæmorrhage*, manifest either as *hæmatemesis* or *melæna*, and in *chronic ulcer* of the stomach or duodenum *producing stenosis* in the body of the stomach or near the pylorus, *dilatation* of the organ, or persisting and intractable dyspepsia. The indications for the treatment of the first of these complications—"perforation"—have been so carefully studied and so definitely set forth by various recent writers that I shall be content with a mere statement of my experience. Of the two latter forms, hæmorrhage and chronic ulceration producing dilatation or inveterate dyspepsia, but little has been written by the surgeon, and I therefore propose to deal with these at greater length and with fuller detail.

1. *Perforation of gastric or duodenal ulcers.*—Perforation may be acute, subacute, or chronic. *Acute* when the ulcer gives way suddenly and completely, and the stomach contents are free to escape at once into the general peritoneal cavity; *subacute* when the ulcer perforates rapidly, but the stomach is empty, the opening small or quickly closed by adhesions or a plug of omentum; and *chronic* when, owing to limiting adhesions to the anterior abdominal wall, the liver, the pancreas, or any neighbouring structure, the escape of contents is slight, and confined by barriers of lymph to a circumscribed area, with the result that an abscess slowly forms and becomes manifest at a later period.

In acute and subacute perforation, an operation should be advised as soon as the diagnosis is assured. In the very great majority of cases the diagnosis is made with confidence, but unless the patient is seen within the first few hours the initial shock may have passed off, especially when morphia has been administered, and it is then difficult to convince one's self of the extreme urgency of the case. The severity of the symptoms depends upon several conditions—the previous state of health, the size and number of the perforations, the condition of the stomach, whether full or almost empty, the bacterial virulence of its contents, and the occurrence of vomiting. The clinical picture presented by an acute perforating ulcer will depend in some measure on the site of the ulcer. If in the fundus, at the cardiac end, or in the body of the stomach an acute infection of the whole peritoneal cavity rapidly follows; if the ulcer be at the pylorus or in the first portion of the duodenum the fluid is directed down the right side of the abdomen, owing to the hillock formed by the transverse mesocolon at the pyloric end of the stomach. The right kidney pouch is filled, and the fluid then escapes downwards into the right iliac fossa, and there accumulating gives rise to symptoms and signs which mimic with extraordinary accuracy those caused by an acute appendicitis. Indeed, in nineteen cases of per-

forating duodenal ulcer out of fifty-one recorded by me in a paper published in the 'Lancet,' the appendix was cut down upon after a diagnosis of acute appendicitis had been made.

One point which seems definitely settled by my experience in operations upon the stomach is the possibility of recovery from subacute, and perhaps even from acute perforation of the stomach without operation. In two cases a diagnosis of perforation of an ulcer had been made by the medical man in attendance. Owing to the inaccessibility of a surgeon, the patients were kept under morphia regularly administered, and rectal feeding was adopted. At the operation innumerable adhesions were found, more especially near the pyloric end of the stomach, and the extent and position of these suggested that they were the result of an intense local inflammation set up by the bursting through of an ulcer of the stomach. Such cases as these, however, only seem to emphasise the importance of early operation in all cases, for the hazard of spontaneous recovery is immeasurable, whereas the risk of operation is definite. Out of the nine cases I have had under my care four patients have recovered. I should consider that this result is as good as one may reasonably expect, when the difficulties of securing the case at an early stage for operation are remembered. If statistics are compiled from recorded cases alone a better impression may be derived than this, but every surgeon knows and has probably experienced himself the desire for announcing his successes, and of quietly postponing any mention of his disasters.

Taking all cases into account, and including those in which death results, perhaps remotely from subphrenic or other perigastric abscess, I should estimate the average recoveries at 35 to 40 per cent.

In operating I do not excise the ulcer. A continuous suture of catgut taken wide of the ulcer, folds the stomach walls over and buries the rent. A second continuous suture of Pagenstecher thread is placed outside

the first. I generally flush the peritoneum, if much soiled, with hot saline solution; if little soiled, I wipe it clean with large swabs dipped in saline solution, and at once used without being squeezed. Drainage is very rarely necessary.

2. *Operations for hæmatemesis and melæna.*—There has been not a little discussion during the last two or three years as to the propriety of surgical intervention in cases of serious bleeding from gastric and duodenal ulcers. My experience has led me to form decided views as to the kind of case in which operation should be advised, and as to the kind of case in which surgical aid is rarely, if ever, necessary.

Hæmorrhage may occur from acute and from chronic ulcers of the stomach, and whereas in the latter form the bleeding may vary within very wide limits, both as regards quantity and frequency, in the former the clinical history is repeated in case after case with the most remarkable monotony.

*Hæmorrhage from an acute ulcer.*—When a severe attack of hæmatemesis occurs from an acute ulcer it is but seldom that we can obtain a history of antecedent symptoms of gastric discomfort. Hæmorrhage is in a large proportion of cases (in 75 per cent. according to Fenwick) the first symptom. If earlier symptoms can be elicited on close inquiry, they are found to have been, as a rule, very brief and trivial, and to have attracted no serious attention from the patient. The amount of blood lost is always large, and it is lost within the space of a few minutes. A pint, a pint and a half, or even more may be ejected in two or three rapidly succeeding efforts. The general symptoms are those attendant upon any serious loss of blood—collapse, more or less profound,—blanching, sweating, rapid shallow breathing, thin and quick pulse. The body surface becomes cold, pallid, clammy; the patient is restless, and complains always and constantly of a thirst which cannot be quenched. If the bleeding ceases, reaction may soon be noticed—the temperature, which had



been depressed, gradually rises, and may reach 100° or 101°, and colour returns to the lips and cheek. Thirst and restlessness generally persist.

As a rule the outburst of hæmorrhage is not repeated, or if repeated is not severe. A mouthful of blood may be brought up once or twice in the course of twenty-four hours, but there is rarely more than this.

The rapidity of the outpouring of the blood may be gauged, with seeming accuracy, by noting the appearance of the vomit; bright fluid blood has escaped rapidly from the bleeding vessels, dark brown blood, or fluid black as ink, has been long stagnant in the stomach, and has been changed in colour by the action of the gastric juice.

*The characteristics, therefore, of the hæmorrhage from an acute gastric ulcer are spontaneity, abruptness of onset, the rapid loss of a large quantity of blood, the marked tendency to spontaneous cessation; and the infrequency of a repetition of hæmorrhage in anything but insignificant quantity.*

*Hæmorrhage from a chronic ulcer.*—In all cases in this group there have been symptoms of chronic indigestion, pain, or fulness after meals, and occasional vomiting for months, or even years, and there is constant complaint of greater discomfort in the later days. The bleeding varies within the widest limits of frequency and quantity, but, speaking roughly, we may say that the cases are divisible into two groups. In the one the hæmorrhage is trivial in amount, capricious in onset, irregularly repeated, and is merely an unexpected and, on the whole, an unimportant addition to the usual attacks of vomiting. From time to time a tinge of blood or even a few ounces may be observed in the food ejected in one of the constantly recurring attacks of vomiting. It is probable that small quantities of blood are not infrequently present in vomited matter, or in the stools, and pass unobserved owing to the absence of symptoms. The estimates given by authors as to the frequency of hæmorrhage in cases of chronic gastric ulcer vary between 20 per cent. and 80 per cent., and this difference is due not so much to the

variations in the disease as to the closeness and accuracy and continuity in the observations made with reference to the constituents of the stomach contents and of the fæces.

In the second group the hæmorrhage is the predominant feature. In a patient who has been subject for years to indigestion there is a sudden attack of hæmatemesis. This attack may or may not be, but in my experience generally is preceded by a notable accession of pain and gastric irritability for, at the least, two or three days. The hæmorrhage is copious, half a pint at the least, and very commonly a pint, being lost. After a quiescent period of twenty-four hours or more a second equally severe attack occurs, to be followed in its turn by a period of quiet which ends abruptly with a sudden and generally a more serious bleeding. In each attack the bleeding is free, but is rarely so copious and overwhelming as in acute ulceration. In rare cases, when a large vessel is opened by the ulceration, the hæmorrhage may be inundating, and cause the almost sudden death of the patient. Such a catastrophe is, however, very unusual. So far as the general effect upon the patient's condition is concerned, it is usually noticed that after hæmatemesis from an acute ulcer a speedy recovery is made. The pulse quickly regains its former good volume, and the effects of the depletion speedily pass off. In the hæmorrhage from chronic ulcer a persisting anæmia is almost constantly observed, and in some cases is an obvious and the most striking feature of the case.

The characteristics, therefore, of the hæmorrhage from a chronic ulcer, omitting the inconspicuous and the immediately fatal cases, are *the onset after a long history of digestive disturbances culminating in acute discomfort for a few days, the tendency to recurrence with brief intermissions of a few hours or a day or two, the moderate quantity of blood ejected in each outbreak, and the condition of profound anæmia produced by the repeated loss of blood.*

It is mainly in regard to the treatment by operation of these forms of hæmorrhage that differences of opinion

have been expressed by physicians and surgeons who have written upon the subject. The most ardent advocate of the early adoption of surgical measures is Dieulafoy, who advises that even in a first attack of hæmorrhage an operation should be performed if half a litre of blood is lost. It seems to me that an approach to a successful solution of this most difficult problem of when to operate may best be made by accepting the distinction between hæmatemesis from an acute and hæmatemesis from a chronic ulcer, and by endeavouring to realise the exact pathological conditions which may be present in each of these varieties.

In those cases of hæmorrhage from an acute ulcer in which an operation has been performed, the conditions found have been differently described. In many, certainly in a majority, the blood has been observed to come from many simple erosions, or superficial pittings on the mucous membrane. It is as though the membrane were quietly "weeping" blood. No spouting vessel has been observed, no single point from which the blood chiefly ran. An abundant oozing from many points is, rather, the type of bleeding seen. The large quantity of blood poured out is due to the multiplicity of the points from which it oozes, and not to the size of any single ulcer. In some a small, round, sharply defined ulcer, or two or more such ulcers have been observed, and excision, or transfixion of the base of the ulcer, or ligature *en masse* has been performed. When multiple points of oozing have been found such treatment has clearly been impossible. Under such circumstances the cautery has been employed, or a styptic has been wiped over the surface, temporary pressure has been made with gauze soaked in some astringent, or, finally, gastro-enterostomy has been performed.

The cases in which a definite bleeding point has been seen and secured, or the ulcer excised, are certainly in a small minority. In the greater number of cases a general oozing has been observed, and some of the measures already enumerated have been adopted.

It is perhaps neither easy nor safe to judge of these cases merely by the reports which have been published ; but taking into account the characteristic features of the hæmorrhage from acute ulcers, and especially the very marked tendency to spontaneous arrest of the bleeding, it is difficult to be convinced that, in these cases of "weeping" mucous membrane, any real benefit has accrued from operation ; the surgical interference seems rather to have been, in the successful cases, a complication in what would otherwise have been an uneventful recovery. The question is one, however, which cannot be settled with the knowledge at present at our command, but I am inclined to think that in acute ulceration hæmatemesis does not offer much scope for satisfactory treatment by the surgeon. If, however, operation is for any reason deemed imperative—as, for example, when the hæmorrhage is both copious and recurring,—it is probable that a gastro-enterostomy speedily performed will be the most appropriate and most successful method of treatment.

In the hæmorrhage from a chronic ulcer the case is far otherwise. In most of the recorded examples an ulcer with densely thickened base and indurated edges has been more or less readily found, in many the bleeding point has been seen and the ulcer excised, or its base transfixed and the ligatures tied. In others a gastro-enterostomy has been done with perfectly satisfactory results. One can readily understand, on examining a chronic ulcer which has bled intermittently, how difficult it is for the hæmorrhage to be checked spontaneously. The base of the ulcer is densely hard, and the vessel traverses it like a rigid pipe. One side of the vessel is destroyed by the ulceration, which makes a ragged hole therein. The vessel is unable, owing to the stiffening by chronic inflammatory deposit, to contract or retract, and the bleeding can therefore only be checked by the plugging of the opening by a thrombus, which may readily be detached or destroyed. In one of the seven cases below recorded, in which the hæmorrhage had been excessive and frequently

repeated, the ulcer was exposed at once; it was on the lesser curvature towards the cardiac orifice. Excision was performed by making an elliptical incision round the base; when the first half of the incision had been made, and the ulcerating surface exposed, the bleeding was readily seen. The wound resulting was stitched up, and gastro-enterostomy was *not* performed. In view of the issue of this case, I much regret that I did not make the short circuit. In the remaining six one or more ulcers were found; in one an ulcer on the posterior surface was excised, and gastro-enterostomy performed to the opening which resulted, and in five a gastro-enterostomy alone was thought necessary. It is a striking fact, though possibly a coincidence, that the only case in which gastro-enterostomy was not performed was the only case I lost. That the short-circuiting is of value in expediting the healing of an ulcer there can be no doubt, but in what way precisely it so acts is difficult to say. The more ready emptying of the stomach is probably the chief and the most important result of the anastomosis, but the avoidance of, or the nullifying of the evil effects of, a pyloric spasm is certainly a factor. To sum up, I would suggest that the treatment of hæmatemesis will depend upon the nature of the ulcer from which the blood is coming. In hæmorrhage from an acute ulcer medical treatment alone will suffice; surgical measures will very rarely be necessary. If any operation has to be done, gastro-enterostomy will probably prove the most effective.

In chronic ulcer operation should be advised as early as possible. If readily exposed and not adherent to the pancreas or other organ, the ulcer, if solitary, may be excised; but a simple gastro-enterostomy is probably sufficient to secure the arrest of the hæmorrhage and the rapid healing of the ulcer.

3. In this third group I have included those cases in which the symptoms depended upon chronic ulceration of the stomach. The chronic ulcer, if situate at or near the pylorus (on either side), causes obstruction and consecu-

tive dilatation of the stomach, and if in the body of the stomach causes inveterate dyspepsia, or hour-glass stomach, and possibly also pyloric obstruction due to spasm. In some instances a wide-spread mesh of adhesions or tough fibrous bands, crippling the stomach in its action, or warping its outline, will be found.

The evidences of old ulceration in the stomach are at times difficult to discover; a slight thickening of the stomach wall, or a few firm adhesions to a puckered area on the anterior or posterior surface, may be all that can be discovered. Yet these are, as my cases indisputably show, enough to cause severe intractable dyspepsia, and to compel in the worst cases a life of invalidism and utter misery. One circumstance that has been repeatedly impressed upon me by my cases is the multiplicity of gastric and duodenal ulcers. It would certainly appear that a gastric ulcer, if chronic, is rarely solitary. Other ulcers are found in the stomach, or in the duodenum. Two ulcers are not infrequently seen in exactly opposing points of the anterior and posterior walls, in such positions that if the stomach were held up and a needle passed through from front to back, the bases of both ulcers would be transfixed. In hour-glass stomach, in addition to the central narrowing a second constriction is often formed at the pylorus, and is due in most cases to a separate ulcer, so that a double operation, to allow of the emptying of both cardiac and pyloric pouches, is necessary.

If an ulcer is bleeding freely it may become, therefore, a difficult question to decide as to which one of two or more palpable ulcers should be excised. When hæmorrhage occurs from an ulcer there has probably been a recent accession of inflammation in the ulcer, deepening it and causing the erosion of a vessel. In such a case a turgid or oedematous appearance, or a reddening, or recent lymph formation on the surface may be found. But whether hæmorrhage is occurring, or whether inveterate dyspepsia is the cause of the operation, the treatment may be the same. Excision of the ulcer is certainly not neces-

sary; a gastro-enterostomy will, without question, suffice to effect the healing of the ulcer, and will give complete relief. In all cases of chronic gastric ulcer, whatever the position of the ulcer may be, I now perform gastro-enterostomy. In three cases in which the pylorus was markedly stenosed I have performed pyloroplasty. One of the three patients is quite well; he has, indeed, been almost as satisfactory as any stomach case that I have treated. The second patient is very decidedly improved, but he still has occasional slight indigestion. The third patient suffered a recurrence of the symptoms in a few months, and I had to perform gastro-enterostomy; since this operation she has been perfectly well. I do not doubt that pyloroplasty is a safe and suitable operation in a certain number of cases where stenosis is due to a long-healed ulcer, and is limited to a narrow ring of the pylorus, but in the majority of cases of pyloric stenosis these ideal conditions are not present. Indeed, it is impossible to tell from external examination alone that the ulcer at the pylorus is healed. In comparison with gastro-enterostomy, therefore, pyloroplasty is less frequently applicable, and is less satisfactory and certain in its results. I do not intend to perform a pyloroplasty in any case in the future, for, even under the ideal conditions mentioned above, a gastro-enterostomy acts on the whole better, and is, properly performed, not liable to be followed by a recurrence of symptoms. Indeed, I do not know any operation in surgery which is more successful, or which is attended by better or more striking results, than gastro-enterostomy for chronic ulcer of the stomach. A patient, thin, shrunken, cadaverous, and gloomy in aspect, who has been chiefly occupied in trying to avoid acute attacks of indigestion or vomiting, whose whole attention is concentrated on his stomach, who considers every article of diet carefully before he takes it, and by degrees abandons first this dish and then the other until he is finally reduced to fluids alone—who, indeed, has never conceived that any other question than that of his own health could seriously

interest him,—a patient, to say the truth, whose whole existence has been ordered and regulated by his stomach, finds, after a gastro-enterostomy has been performed for his chronic ulcer, that he can eat what he likes, in any quantity he likes, that he rapidly puts on weight, and that his general sense of well-being is almost beyond belief. From being a misanthrope he becomes an enthusiast and an optimist. I have often wondered, with a certain amusement, what would have been the result of a timely gastro-enterostomy upon Thomas Carlyle. He might have taken to the writing of comedies, and threatened the throne of Congreve. And his portrait twelve months after the operation, viewed side by side with that done by Whistler, would have proved an eloquent advertisement for his surgeon.

Since I first performed gastro-enterostomy I have used Murphy's button and Laplace's forceps to aid in the anastomosis, and have united the jejunum to the anterior and to the posterior surface of the stomach. In all the later operations I have used the simple suture, and have performed the posterior operation after the method of von Hacker. I may briefly describe the steps of the operation. The abdomen is opened to the right of the middle line, and the fibres of the rectus are split. On opening the peritoneum a complete examination of the whole stomach and duodenum is made. The importance of this cannot be over-emphasised. A constriction in the body or towards the cardiac end may be most readily overlooked, especially when, as is not uncommonly the case, a marked constriction at the pylorus, seen at once, is ample to account for all the symptoms. Cases of hour-glass stomach which have been overlooked at the operation, and a futile anastomosis made between the pyloric pouch and the jejunum, are recorded by several distinguished operators, and the mistake is an easy one to make unless a determination is made to examine the whole of the stomach in every case. As soon as the operator is satisfied as to the conditions which exist, the great omentum and



transverse colon are lifted out of the abdomen and turned upwards over the epigastrium. The under surface of the transverse mesocolon is exposed, and the vascular arch formed mainly by the middle colic artery is seen. A bloodless spot is chosen, a small incision made in the mesocolon, and the finger passed into the lesser sac. The opening in the mesocolon is then gradually enlarged by stretching and tearing until the whole hand can be passed through it. It is very rarely necessary to ligature any vessel. The hand of an assistant now makes the posterior surface of the stomach present at this opening, and the surgeon grasps the stomach and pulls it well through. A fold of the stomach, about three inches in length, is now seized with a Doyen's clamp. The clamp is applied in such a way that the portion of the stomach embraced by it extends from the greater curvature obliquely upwards to the lesser curvature and towards the cardia. The duodeno-jejunal angle is now sought, and readily found by sweeping the finger along the under surface of the root of the transverse mesocolon to the left of the spine. The jejunum is then brought to the surface and a portion of it, about nine inches from the angle, is clamped in a second pair of Doyen's forceps. The two clamps now lie side by side on the abdominal wall, and the portions of stomach and jejunum to be anastomosed are well outside the abdomen embraced by the clamps. The whole operation area is now covered with gauze wrung out of hot sterile salt solution, the clamps alone remaining visible. A continuous suture is then introduced uniting the serous and subserous coats of the stomach and jejunum. The stitch is commenced at the left end of the portions of gut enclosed in the clamp, and ends at the right. The length of the sutured line should be at least two inches. In front of this line an incision is now made into the stomach and jejunum, the serous and muscular layers of each being carefully divided until the mucous membrane is reached. As the cut is made the serous coat retracts and the mucous layer pouts into the incision. An ellipse of the mucous

membrane is now excised from both stomach and jejunum, the portion removed being about one and three-quarter inches in length and half an inch in breadth at the centre. The stomach mucosa shows a marked tendency to retract; it is therefore seized with a pair of miniature vulsella on each side. No vessels are ligatured. The inner suture is now introduced. It embraces all the coats of the stomach and jejunum, and the individual stitches are placed close together and drawn fairly tight so as to constrict all vessels in the cut edges. The suture begins at the same point as the outer one, and is continued without interruption all round the incision to the starting-point, where the ends are tied and cut short. It will be found that there is no need to interrupt the stitch at any point, for there is no tendency on the part of the sutured edges to pucker when the stitch is drawn tight. The clamps are now removed from both the stomach and the jejunum in order to see if any bleeding point is made manifest. Very rarely, about once in ten cases, a separate stitch at a bleeding point is necessary. The outer suture is now reassumed and continued round to its starting-point, being taken through the serous coat about one sixth of an inch in front of the inner suture. This outer stitch is also continuous throughout; when completed the ends are tied and cut short as with the inner stitch. There are thus two suture lines surrounding the anastomotic opening; an inner, hæmostatic, which includes all the layers of the gut; and an outer, approximating, which takes up only the serous and subserous coats. For both stitches I use thin Pagenstecher thread. No sutures are passed through the mesocolon and stomach. The gut is lightly wiped over with a swab wet in sterile salt solution, the viscera returned within the abdomen, and the parietal wound sutured layer by layer. When the patient is replaced in bed the head and shoulders are supported by three or four pillows. The operation lasts from beginning to end about thirty to thirty-five minutes, but can be shortened by five or ten minutes if the condition of the patient

demands it. Speed in this as in all other abdominal operations is desirable, but is to be distinguished from haste. Speed should be the attainment, not the aim of the operator. With regard to the after treatment there is but little to say; nutrient enemata are given every four hours, and the bowel is washed out every morning with a pint of hot water; no fluid is given by the mouth for twelve hours, or until the ether sickness is over; then water in teaspoonful doses every fifteen minutes is given, and the quantity increased and the intervals lessened if sickness is not aroused. At the end of forty-eight hours milk and a little pudding, soups, and such like are given. By the eighth day fish and minced chicken are taken, and in less than a fortnight solid food will be relished. The patient generally requires a caution not to over-eat during the first month or two, for often the appetite is ravenous.

Regurgitant vomiting has been observed in three cases. In the first, No. 22, it was trivial, it ceased after the stomach had been once washed out; in the second, No. 30, it was greatly lessened by lavage, though the patient had for two months an occasional sudden attack of copious vomiting. A very large quantity of bile was brought up without discomfort, the appetite remained excellent throughout, and the patient gained four and a half pounds in the first three months. This last case is the least satisfactory of all my stomach operations. I asked him three months after the operation whether he considered it had been worth his while to undergo it, and he replied at once, "I'd have it again to-morrow." His relief from pain, his ability to eat any food in any quantity, his general improvement in weight and health, more than compensated for his occasional painless attacks of bilious vomiting. So far as I know there was no difference in this operation from any of the others, and unless the adhesions which tied the pyloric end of the stomach to the transverse mesocolon are responsible for altering the position of the anastomosis, I am at a loss to account for the regurgitation.

In the third case, No. 46, the stomach was universally adherent, both anterior and posterior surfaces were covered with adhesions. The history of the case showed unmistakably that the perforation of an acute ulcer had occurred two years before. The posterior surface of the stomach was certainly less adherent than the anterior, and I therefore performed my usual operation of posterior gastro-enterostomy. After the completion of the anastomosis I was much dissatisfied with the appearance of things; the jejunum did not seem to "sit" nicely. The opening into the distal loop seemed on a higher level than that into the proximal, and I was disposed there and then to perform an entero-anastomosis between the afferent and efferent limbs. I did not do so, but when the vomiting of pure bile came on, as I had anticipated, I reopened the abdomen at the end of fifty-four hours and performed the entero-anastomosis. One hundred and thirty-four ounces of bile-stained fluid had been vomited between the completion of the first and the beginning of the second operation; after completing the second I passed a stomach-tube and emptied out twenty-two ounces more, making a total of 156 ounces which had escaped into the stomach in fifty-four hours. After the jejuno-jejunostomy there was no vomiting at all.

This case has shown me clearly that an error in the proper adjustment of the anastomosing loop is an undoubted cause of regurgitant vomiting. In such a case I should in the future certainly prefer Roux's operation, the "gastro-enterostomy in 'Y,'" to any other. After a perforating ulcer has healed, adhesions, which are universal and bewildering in their complexity, may form. If one surface, anterior or posterior, is free from adhesions, that should be selected for the anastomosis; if both are involved I should prefer the posterior. A stomach so warped by the puckering and contraction of adhesions may, however, alter its shape and position under the new mechanical conditions following upon the gastro-enterostomy, and a subsequent alteration may occur in an anastomosis which at the time seemed correctly made.

To avoid any risk of immediate or future regurgitant vomiting, I should in such circumstances perform Roux's operation, and thereby avoid any possibility of accident.

My experience is much more favourable than that of most surgeons in this matter. Mikulicz, for example, lost seven cases out of seventy-four from regurgitant vomiting. In seven more an entero-anastomosis was performed, and of these three died. I attribute the infrequency of regurgitant vomiting to two details in the operation: first, the obliquity of the opening into the stomach, the lowest part of the opening leading into the distal loop of the jejunum, so that with the patient propped up in bed fluid gravitates into the small intestine; and second, the removal of the mucous membrane, which results in the opening keeping patent, and prevents a pouting of the cut edge of the mucosa from narrowing, or even blocking the opening.

In connection with the operation of gastro-enterostomy the following points are worthy of attention:

1. The sterilisation of the mouth, stomach, and jejunum. As soon as the patient is admitted for operation the preparation of the mouth is begun, the teeth are cleansed and brushed frequently with Condy's fluid; all food given is liquid and sterile. The stomach is washed out twice, once about thirty-six hours before the operation, and again about six hours before, with tepid boiled water. Calomel is given forty-eight hours before the operation.

2. Gloves made of thin india-rubber and boiled are worn by the operator, assistants, and nurses.

3. The hands are rinsed in salt solution during the operation; no antiseptic is allowed to touch the peritoneum.

4. Scrupulous care is taken to avoid any possible infection from the stomach or jejunal mucosa. The scissors and clips which touch the mucous membrane are at once laid aside, and not used during the subsequent stages of the operation. As soon as the mucous membrane suture is completed the gut is lightly washed with saline solution, and the hands are then thoroughly well cleansed.

The following are the notes of the case in which I performed excision of the ulcer. The other cases operated upon for hæmatemesis or mælæna are marked [H] in the tabulated list.

*Diagnosis—Acute Hæmatemesis ; Excision of Ulcer ;  
Gastroplasty.*

July 10th, 1902.—M. P—, aged 18 years. Four years ago had scarlet fever. Since then has never been quite robust. Has suffered at times from pain after food and vomiting. These would be present for two to three days, then would abate, and he would be quite well for a few weeks. Has been careful in his diet. An ordinary hearty meal would invariably arouse the symptoms. Had no hæmatemesis.

On July 6th eat an ordinary breakfast, late in the morning felt ill, epigastric pain and vomiting. At first vomiting seizure only food came back ; at the second a "quart of blood." Later in the day vomited blood—a pint and a half—measured by his doctor. On the 7th vomited blood twice, on each occasion over a pint of clot ; on the 8th, twice ; on the 9th, three times ; on the 10th, once in large quantity and once in small. When I saw him he was very blanched, his face waxen and sweating. The pulse was 114, very thin and feeble. He had been free from abdominal pain since the attack of vomiting. The hæmorrhage had told upon him severely. The persistence of symptoms of gastric ulcer for four years, with hæmatemesis of five days' duration, made the diagnosis chronic gastric ulcer, with recent deepening of the ulcer. It was probable that the bleeding from a dense indurated area would not stop spontaneously. I therefore advised operation.

The abdomen was opened through the right rectus muscle. Almost at once a hard patch about the size of a shilling was felt in the anterior wall of the stomach, near the lesser curvature towards the cardiac end. This was

the ulcer. An incision made by the side of this showed the ulcer in the act of bleeding. The ulcer was cut out by two elliptical incisions enclosing it. The horizontal wound thereby resulting was closed transversely. A careful examination of the rest of the stomach was made, but nothing abnormal found. The abdomen was closed in the usual manner.

TABLE I.—Cases of Perforating Gastric and Duodenal Ulcer.

Name and date.	Sex.	Age.	Symptoms and description.	Condition found ; operation.	Result.	Remarks.
S. A., April 30th, 1897	F.	39	Was admitted with a history of acute onset of severe abdominal pain, chiefly in the epigastric region. There was faintness, followed in about half an hour by vomiting; no hæmatemesis. The abdomen gradually became distended, and the pulse gradually became quicker and feebler. During last year was under treatment by Dr. Bennett for gastric ulcer. Since then has constantly had dyspepsia, pain in the back and epigastrium, and occasional vomiting, but not recently of blood. On Saturday, May 22nd, at 2.30 a.m., suddenly roused from sleep by intense epigastric pain, felt faint, and vomited. Collapse continued, and soon distension and tenderness; vomiting was persistent.	Abdomen opened and a very small gastric ulcer near lesser curvature found to have perforated. There was free effusion, and some curdled milk was seen in the peritoneum. Suture of ulcer, lavage and drainage. Abdomen generally distended, upper part especially; very tense pulse, only just perceptible, cold, clammy hands, livid skin. Operation 11.25 p.m. Large perforation, $\frac{1}{4}$ in. in diameter, just below lesser curvature, nearer cardia	E.	Infirmery. Time after perforation about 30 hours.
M. P., May 22nd, 1897	F.	27	Was under Dr. Johnstone some months ago for indigestion; with dieting, etc., the symptoms abated. No discomfort recently. On Nov. 18th, 5.30 p.m., while at tea, sudden pain, overwhelming, localised beneath ribs on left side, "as though a knife were run in." Abdomen gradually distended. Remained collapsed for several hours, but improved after morphia. No liver dulness. Tenderness over appendix region chiefly	Operation Nov. 20th, 12 noon. Large ulcer easily admitting the middle finger about three inches from cardia on anterior surface. General peritonitis, large collection of thick turbid fluid and lymph	D. in 23 $\frac{1}{2}$ hours	Dr. Bennett, Odley. Died 2.40 p.m. Time after perforation 21 hours.
R. S., Nov. 16th, 1898	F.	20				Dr. Johnstone, Ilkley. Time after perforation about 42 hours.



T. H., April 24th, 1900	M. 44	Symptoms had been present for 18 months; the chief of them was pain two, three or four hours after food. Blood had been observed when the patient vomited; vomiting was frequent but irregular. There was no melena. On April 25th, while in the infirmary, the man became suddenly worse; pain came on acutely in the whole abdomen. Distension and rigidity were soon observed; collapse was pronounced; respirations 28; pulse 128	A diagnosis of perforating ulcer was made and the abdomen opened. The ulcer was found at the beginning of the second part of the duodenum, its diameter was about $\frac{1}{4}$ of an inch. After stitching the ulcer up the gut seemed narrowed to at least half its diameter. A gastro-enterostomy with the aid of a Murphy button was therefore performed. The patient never rallied from his collapse	D.	Dr. Veale, Drighlington. Time after perforation about 26 hours.
M. L., May 12th, 1901	F. 28	Symptoms of indigestion for 8 years. On April 11th was suddenly seized with acute abdominal pain, about 3 hours after breakfast. On admission to the infirmary she was found to be in very acute pain, the abdomen, especially in the upper half, being much distended and very rigid. The epigastric region was excessively tender	An ulcer equal in size to the end of a lead pencil found near lesser curvature, towards the cardia. The stitches held imperfectly until taken very wide of the ulcer. To give security an omental flap was stitched over the ulcer. The early course was satisfactory, but later the temperature ran up and a subphrenic abscess and multiple suppuration in the abdomen resulted, and the patient died May 7th	D.	Infirmary. Time after perforation 28 hours.
L. T., May 5th, 1901	M. 23	Has had symptoms of gastric ulcer for several months. He is a policeman, and has recently been on night duty; frequently has vomited during the night. On morning of May 23rd, 1901, a sudden acute attack of pain and vomiting, when going on duty; he returned to bed, felt ill and cold all day, and at night first sent for a medical man. The abdomen was then distended, rigid, and tender; pulse 124, thin and feeble	An ulcer on the anterior surface, near the pylorus, had perforated. There were masses of lymph between the liver and the stomach. Fluid was found everywhere in the peritoneum. The ulcer was about the size of a sixpence	D.	Dr. Exley, Leeds. Time after perforation 35 hours. Vomiting of digested blood continued for 2 days; it was very acid, and caused redness of the cheek and chin. At the post-mortem two other acute ulcers found.

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
June 18th, 1901	M.	25	The patient, a sturdy robust labourer, stated that for about 4 weeks before admission he had suffered from indigestion and vomiting. On June 18th, while climbing a ladder, was suddenly seized with intense abdominal pain. He was seen at once by a medical man who happened to be near, and sent to the infirmary. He was then profoundly collapsed, breathing quick and short; pulse 128, abdomen rigid and unyielding. A diagnosis of perforated ulcer was made.	A perforation equal in diameter to a No. 8 or 9 catheter was found in the duodenum 1 inch from the pylorus. The ulcer was stitched and the abdomen cleansed and drained	R.	Infirmary. Time after perforation 3 hours 50 minutes.
R. H., March 13th, 1902	F.	24	Was married 8 weeks ago. Had suffered slightly before that from indigestion, but never severely. Thirty-six hours before operation was suddenly seized with acute intolerable pain underneath the left costal margin. There was no vomiting, but faintness and collapse were pronounced. Gradually the abdomen began to distend, and the pulse to fall. On examination the abdomen was distended uniformly, and was everywhere tender. In the left upper quadrant, beneath the left rectus, a specially tender area	An ulcer near the cardia had perforated. The edges for at least an inch round were solid and hard, and stitches cut through when tightly tied. An area of stomach was infolded, and an omental flap stitched like a lid over the line of suture. There were large masses of thick lymph for a few inches round the ulcer	R.	Dr. Bates, Ilkley. Time after perforation about 38 hours.
I. S., Reg. No. 1825, April 20th, 1902	F.	17	For several weeks had had slight indigestion and epigastric pain, but not in sufficient severity to send her to a doctor. Last night, April 19th, at 9 p.m., a sudden attack of acute epigastric pain; morphia given. Seen at 7 a.m., abdomen very rigid and rather tender, especially over gall-bladder. Has vomited once. Pulse 112. Very shallow respiration	An ulcer perforated on anterior surface of duodenum about $\frac{3}{4}$ inch from pylorus. Some fluid above the stomach. Ulcer closed by suture; peritoneum cleansed by wiping with swabs wet with sterile salt solution. No lavage, no drainage	R.	Infirmary. Time after perforation about 10 hours.

TABLE II.—*Gastro-enterostomy for Simple Diseases—Chronic Ulcer of Stomach and Duodenum ; Pyloric Stenosis ; and Dilated Stomach.*

Name and date.	Sex.	Age.	Symptoms and description.	Condition found ; operation.	Result.	Remarks.
E. B., Jan., 1900	F.	41	At age of 16 had an illness, attended with the vomiting of blood on one occasion in large quantity. Pain after food ever since ; at times better, at times worse. Diet has been carefully and rigidly supervised. In June, 1899, pain began to be much more acute, and vomiting, which before had been inconstant, now became frequent ; large quantities (4 pints) were vomited. On examination of abdomen a large contracting stomach seen ; nothing abnormal felt over pylorus	Thickening at pylorus and along first portion of duodenum, with contraction and many adhesions. The adhesions were carefully broken down. A gastro-enterostomy was performed with the aid of Laplace's forceps, the operation being very simple and speedy	R.	Quite restored to health ; eats well, and suffers no pain. July 29th, 1902.—Quite well ; in "first-rate health."
F. S., Feb., 1900	M.	35	Prolonged symptoms of chronic ulceration of stomach with hyperchlorhydria. Under medical treatment (bismuth and morphia about two hours after meals, etc., etc.), he improved for a time, but eventually treatment induced no improvement. Since June, 1899, has been steadily losing ground. Pain and vomiting severe and disabling and of daily occurrence. On examination a large and contracting stomach	Very dilated stomach with pyloric contraction, some thickening, and many adhesions. Gastro-enterostomy with Laplace's forceps	R.	Has been very well since the operation. Has gained (July, 1902) about 1 stone in weight.

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
A. B., Jan., 1900	M.	55	Dyspepsia for 10 or 12 years, culminating 5 years ago in an "attack" which lasted two weeks and was remarkable for the severity and continuance of epigastric pain and the persistence of vomiting. Since this attack has had periodic seizures of copious vomiting at intervals of 24 hours to 3 weeks. Pain after food at intervals of 3 to 6 hours, varying greatly in severity, but generally not amounting to more than discomfort. On one occasion in hospital the vomited matter measured 5½ pints. The stomach was huge and flabby, but contractions were always visible. HCl present	Enormous stomach. When distended with two seidlitz powders, the outline of the greater curvature descends behind the symphysis pubis. An ulcer was found extending outwards into the duodenum; cicatricial contraction very marked; adhesion to liver. Gastro-enterotomy by the aid of Laplace's forceps and separation of old adhesions	R.	Patient reports (August, 1902) himself "as well as ever he was in his life, and able to eat anything."
<p><sup>1</sup> This patient returned to hospital in March. After operation there was considerable relief for about a month. Then, after a heavy meal consisting largely of boiled peas, there was an attack of pain and vomiting, and from that date the symptoms gradually returned. On admission his condition was practically the same as before operation. The abdomen was again opened, and a second gastro-enterostomy, with the aid of Murphy's button, performed. The opening made at the first operation, between the stomach and intestine, was practically closed. Patient made a good recovery. When seen in September, 1900, he said he was "never better in his life, and gained over 2 stones in weight, and had no gastric anxieties or discomforts."</p>						
S. H., Aug. 1st, 1900	F.	40	Nine months ago first noticed pain in epigastric region after eating; 5 months ago first vomited; pain and vomiting speedily increased in frequency and severity. Now the pain commences about 1 or 2 hours after food, and continues until vomiting	Hard cicatricial ring at pylorus, a few adhesions to liver; the finger invaginating the anterior wall of the stomach feels and recognises the pyloric orifice merely as a dimple. Posterior gastro-	R.	"Complete relief." Report, July, 1902.—Is perfectly well, and can eat and digest ordinary food.

F. H., June, 1900	32	M.	comes on spontaneously or is induced. No blood has ever been noticed in the vomit. No solid food has been taken for 2½ months; the chief diet obvious on examination. On distension below the umbilicus and contractions. Symptoms of ulcer; "acid dyspepsia." 10 months ago. Relieved for 1 month by bismuth and morphine. For 7 months severe pain after food, worse about 2 hours after a meal. Vomiting every 2 or 3 days up to 3 months ago, since then almost daily. Stomach dilated and contracting. Lost 2 stones in weight. Free HCl	enterostomy by suture, without mechanical appliances	is milk and soda. Considerable wasting. A dilated stomach is distended by seidlitz powder, the greater curvature descends 2½ inches below the umbilicus and contractions. Symptoms of ulcer; "acid dyspepsia." 10 months ago. Relieved for 1 month by bismuth and morphine. For 7 months severe pain after food, worse about 2 hours after a meal. Vomiting every 2 or 3 days up to 3 months ago, since then almost daily. Stomach dilated and contracting. Lost 2 stones in weight. Free HCl	R.	Has regained lost weight, and can eat heartily without discomfort.
T. H., June 6th, 1900	52	M.	For several years has suffered from indigestion. During the last six months has suffered acutely, pain and vomiting have become increasingly frequent. He has lost 3½ stones, and looks pinched and ill. The stomach is very largely dilated, and is easily seen contracting. Free HCl is present	A thick tough mass at the pylorus, densely adherent. A few enlarged glands near the tumour. Anterior gastro-enterostomy	R.	Dr. Clarke, Doncaster. Weight before operation 7 stones. Dr. Clarke writes on July 6th, 1902, "I saw T. H. this morning, looking well. He now weighs 10½ stones, his old weight. He is doing his ordinary work, and is in splendid health." Dr. La Touche, Ossett. In July, 1902, this patient was in good health, very stout, and "the wonder of the country side." The tumour was thought to be possibly malignant.	
A. C., Jan. 15th, 1901	52	F.	Menopause five years ago. Since then has been subject to attacks of vomiting, increasing in frequency and severity; vomited blood at the beginning of these attacks, but not lately. Pain after food constantly, generally 1 to 2 hours after. Is relieved by vomiting. On examination a very dilated stomach, with obvious contractions. On filling with CO <sub>2</sub> stomach is seen to descend 1 inch below umbilicus. Free HCl. Traces of lactic acid. Oppler-Boas Vicilli. No tumour felt	A large pyloric tumour, with many adhesions, especially behind gland, felt at head of pancreas and along the lesser curvature. Removal found quite impossible. Posterior gastro-enterostomy	R.		

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
W. B., Feb. 22nd, 1901	M.	60	Had an "ulcerated stomach" 20 years ago; gastric uneasiness ever since. During last 2 years has been under constant treatment by many doctors. Pain severe and constant, increased by solid food, in epigastrium, radiating round and through left side to back. Very rarely vomits; stomach dilated, no wave-like contractions observed. Is said to have passed tarry motions. Has lost weight (2 st. 9 lbs.), taken only liquids, very little of them. Free HCl, a trace. A trace of lactic acid. Diagnosed malignant disease implanted on ulcer.	Stomach a little dilated; quite close to pylorus on the anterior wall an ulcer equal to a shilling in size, with puckering of serous coat, a little thickening and induration, but clearly not malignant. Posterior gastro-enterostomy	R.	Sent by Mr. Stansfield. Weight at operation 8 st. 8 lbs. June 5th.—10 st. 3 lbs. September, 1902.—10 st. 8½ lbs.
L. S., Feb. 19th, 1901	F.	31	For several years attacks of gall-stone colic. Seven months ago removal of stone impacted in cystic duct. Uneventful recovery from operation. Since then symptoms of dilated stomach; copious vomiting at intervals of 2 or 3 days. Pain, uneasiness, feeling of distension after food. Stomach below umbilicus; waves seen without distension with CO <sub>2</sub> .	Large stomach. Innumerable tough adhesions between gall-bladder, abdominal wall, and stomach. Impossible to liberate them, so gastro-enterostomy was performed	R.	Dr. Waugh, Skipton (Hospital), September, 1902. —Quite well; eats heartily, and has absolutely no pain.
E. W.	F.	27	Has been continuously under medical treatment for nearly 2 years. Suffers from pain before food, when stomach is empty, and after taking food in anything but very small quantities. Pain when fasting is relieved by a drink of milk and a small biscuit;	An ulcer equal in size to a shilling about 1 inch from pylorus. During the operation a marked circular contraction of stomach at the site of ulcer was seen. The stomach seemed as though	R.	Dr. Waugh, Skipton (Hospital), September, 1902. —Very well indeed. Has made a perfect recovery

<p>S. B., Feb. 16th, 1901</p>	<p>F. 31</p>	<p>anything more causes pain after an interval of 4 hour. Vomiting has been occasional; no blood. Has been kept at rest and dieted for a long period without any result. Tenderness in epigastrium; distension slight</p> <p>For some years has had pain after food, and diarrhoea. For last 5 to 6 months pain has been much more severe after every meal. It comes on about 1/4 an hour after food, and lasts for 3 hours or more. Vomiting is infrequent unless self-induced to obtain ease. On two occasions has noticed blood, but only in small quantities. Has lost health and strength, and has thinned. Continuous treatment for 5 months has proved unavailing. Tenderness on pressure over pylorus. Doctor writes, "Had tried all the usual drugs without relief, that nothing could be taken without great pain, and she was losing flesh and strength." Stomach a little dilated, five years ago an operation was performed for removal of gall-stones. There were many adhesions round the pylorus. For 2 years had symptoms of pyloric obstruction, for which posterior gastro-enterostomy was done by a colleague, Murphy's button being used. For over a year was very much better. Then symptoms returned. Vomiting copious; pain intolerable. Diet limited to thin fluids. On examination the stomach was dilated to left of umbilicus, and seemed anchored towards pylorus</p>	<p>R.</p>	<p>Three ulcers found; two in stomach near lesser curvature, one about an inch from pylorus, the second 2 1/4 inches, one in first part of duodenum, with considerable induration. Posterior gastro-enterostomy by simple suture</p>	<p>Dr. Lockwood, Halifax. Made a good recovery. When seen 3 months after the operation had gained 10 lbs. in weight.</p>
<p>M. B., Feb. 5th, 1902</p>	<p>F. 56</p>	<p>Dr. Hick. Weight 7 st. 6 lbs. Feb. 6th, 1902—8 st. 5 lbs. Takes food well, no pain; "highly satisfied."</p>	<p>R.</p>	<p>The peritoneum was with difficulty opened, owing to the numberless and dense adhesions, which were quite bewildering. The posterior surface of the stomach was adherent to the anterior abdominal wall at place of former anastomosis. A second wide anastomosis was now made immediately beyond the first one. On introducing one finger into the stomach and another into the jejunum the first opening was found to be almost or completely closed</p>	<p>Dr. Hick. Weight 7 st. 6 lbs. Feb. 6th, 1902—8 st. 5 lbs. Takes food well, no pain; "highly satisfied."</p>

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
M. H., Feb. 12th, 1901	F.	22	Indigestion for 9 months quite intractable. Began with a severe attack of pain accompanied by vomiting, lasting 3 days; blood noticed in vomit during first day. Since then pain always after food, generally 1½ hours after, radiates to right shoulder. Vomits frequently but at very irregular intervals. She has had biliousness and morphia, and much medical treatment, but absolutely without more than temporary benefit. Stomach down to umbilicus and splashy. Symptoms began "12 months ago." Pain in body after meals, which had been trivial for many years, became then troublesome, generally felt about 1½ hours after food. Radiated round side to the back. Vomiting every day or two as a rule. On a few occasions did not vomit for days. Has noticed blood once only. Very rigid and tender over pyloric area. Stomach dilated to right below umbilicus. Free HCl	Stomach dilated as result of an ulcer about 1½ inches on cardiac side of pylorus; much induration and a few adhesions to abdominal wall and gall-bladder. Posterior gastro-enterostomy by suture.	R.	Dr. Milne Mirfield. Has been seen at intervals since; can take ordinary food in any quantity.
M. A. G., Nov. 2nd, 1901	F.	44	Symptoms began "12 months ago." Pain in body after meals, which had been trivial for many years, became then troublesome, generally felt about 1½ hours after food. Radiated round side to the back. Vomiting every day or two as a rule. On a few occasions did not vomit for days. Has noticed blood once only. Very rigid and tender over pyloric area. Stomach dilated to right below umbilicus. Free HCl	Large stomach. Puckering and induration on posterior surface of pylorus, adherent to pancreas. Posterior gastro-enterostomy	R.	Dr. Clements, Farpley. September, 1902.—"Quite well, and very grateful for what has been done."
M. P., March 16th, 1901 [H]	M.	30	Symptoms 5 or 6 years. Pain in epigastrium after meals, most severe in bed at night; slight pain between shoulders. Vomiting for 12 months, almost regularly on alternate days. "Watery pulegm, very sour," once blood. Lost nearly a stone in weight. Always careful in diet. Has attacks of faintness, prostration, and melena	Ulcer in 1st portion of duodenum, with many adhesions. Small scar of gastric ulcer on posterior surface. Posterior gastro-enterostomy	R.	Dr. Millhouse, Dr. Anning. May 31st, 1901.—Gained 12 lbs.; eats well; no "attacks" since operation.



M. C., April, 1901	48	Under medical treatment 5 years with stomach disorder. Has been carefully dieted; still is always expecting and generally has pain, distension, uneasiness after food. Has bled freely several times recently. Stomach dilated. The symptoms since Christmas have been those of Reichman's disease. Hyperchlorhydria. The recent occurrence of severe hemorrhage necessitating rest for 2 or 3 days in bed has alarmed him. The attacks have left him anemic and prostrate, and he has lost over a stone in weight	R.	Large ulcer at least size of a florin on the posterior surface near the pylorus. A scar of a smaller ulcer is seen on posterior surface, about 3 inches from the pylorus. Posterior gastro-enterostomy. Owing to stoutness and rigidity of muscles, I was hampered during the operation, and made a smaller opening than usual.	Dr. Ellis, Halifax. A ventral hernia in upper part of scar. A Pagenstecher thread with which I stitched up the abdominal wall suppurated and discharged itself. Report, August, 1902, "in robust health."
W. K., April 29th, 1901	59	Soldier 25 years. Has been ill 2½ years. At first loss of appetite, indigestion, and flatulence. Has attacks of severe pain, limited to upper right quadrant of abdomen, followed by vomiting. These come 2 or 3 times a week; vomiting always relieves them. Has lost 4 stones. On two occasions (June, 1899 and March, 1901) has vomited much bright blood. On last occasion melana also noticed. Stomach descends to within 2 inches of the pubes, and is seen actively contracting	R.	A hard mass at pylorus and a thickening of head of pancreas (probably simple, though possibly malignant). Stomach shows scars of 3 ulcers. Posterior gastro-enterostomy. An example of chronic pancreatitis, due to gastric or duodenal ulcerations	Dr. Basil Housman, Edgeley, Stockport. Weight, 8 st. 5½ lbs. June 26th.—Gained 31 lbs. and perfectly free from pain. Died of pneumonia in December, 1901. Was better in health before this than for many years. "The pyloric tumour had disappeared. He could eat and digest anything, and was quite a hearty man" (Dr. Housman).
E. J., May, 1901	48	"Gastric ulcer," 1889. Since then digestive disturbances. Pyloroplasty in January. Complete relief for about 5 weeks; then return of all symptoms. Very tender and rigid beneath upper part of right rectus. Hematemesis 3 times recently	R.	Much induration and thickening at pylorus, with some adhesions. The ulceration had widely extended. Posterior gastro-enterostomy	Dr. E. R. F. Mason Hill, Gomersal. Was quite well after gastro-enterostomy.

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
Mrs. H. June 20th, 1901	F.	37	Has had indigestion for 20 years. Pain after food; vomiting at intervals of 4 days at the longest. Never has a "good meal;" cannot eat solid food. Five years ago an acute attack of vomiting lasting several days. A similar attack 17 or 18 months ago. On both occasions blood was noticed. She says, "I've no pleasure in living, and can't go on as I am." Stomach dilated to 2 inches below umbilicus, faint waves. No gurgling or forcing sounds. A thin, sallow, dyspeptic woman.	Dilated stomach. Three distinct scars on anterior surface; one at pylorus with much induration and omental adhesions; two on stomach side of that. A few adhesions on the posterior surface. Posterior gastro-enterostomy	R.	Dr. B. W. Housman, Edgeley, Stockport. Weight before operation, 5 st. 11½ lbs. Weight April, 1902, 6 st. 10 lbs. In September, 1902, Dr. Housman writes, "Can enjoy any ordinary food, and is in complete comfort. She is very grateful indeed."
A. H. July 11th, 1901	F.	24	Has had characteristic symptoms of gastric ulcer for about 18 months. For the last 6 months has been kept in bed under medical treatment, but has vomited almost daily, and on all occasions blood in greater or less quantity has come. Is very pallid and anæmic. In hospital she vomited daily fresh and partially digested blood. She is very much blanched, has attacks of fainting in bed, and looks very ill	An ulcer close to pylorus, with thickening over an area the size of a shilling. A dense, hard area with red-dened surface and edges covered with lymph on the posterior surface. Posterior gastro-enterostomy; an ulcer, probably the bleeding one on posterior surface, being excised and opening left united to the jejunum	R.	Dr. Clarke, Wakefield. Was in the Manchester Union Infirmary in 1902. Was said to have recently had attacks of vomiting, but when carefully watched no vomiting was observed, and she was discharged.
N. W., Aug. 1901	F.	28	Stomach trouble since 12 years old. Pain after food and vomiting; never hæmatemesis; no melenæ. If she takes a meal now feels full and uncomfortable for about 1½ hours, then pain, generally becoming acute, leads to vomiting, which gives ease	Ulcer from near pylorus on greater curvature; a few adhesions. Very large flabby stomach, the pancreas seen above the lesser curvature	R.	Dr. F. W. Robinson, Huddersfield. Had slight regurgitant vomiting for 12 days, relieved by first washing out of stomach; no feeling of sickness after. Rapidly gained

T. T. Nov. 2nd, 1901	M.	40	Constant unease. Stomach dilated and proptosed	Symptoms began in June, 1900, burning pain and vomiting after food, generally $\frac{1}{2}$ hour after a meal. No hematemesis. Two months ago an attack of vomiting lasting 2 days; extreme irritability of stomach. No melena. On examination a huge stomach, contracting. Free HCl. Loud gurglings at pylorus. Has had severe cramps in muscles of neck and extremities. Tetany	Enormous stomach. Several ulcers (5 well marked) in stomach, and one just beyond the pylorus. Posterior gastro-enterostomy	R.	health and strength. In August, 1902, "very well indeed."
F. D. Nov. 30th, 1901	F.	19	Twelve months ago began to have pain after food, coming generally about $\frac{1}{2}$ hour after a meal, and increasing in severity for 2 hours. This is increasing in severity, and is now extreme and disabling. Constant feeling of sickness after food, and retching; vomits only every week or 10 days, and then in copious quantities. No hematemesis and no melena. On examination a dilated stomach to $1\frac{1}{2}$ inches below umbilicus. Free HCl. Lavage and medicines have been tried for 4 months without any benefit	Very dilated stomach, a scar of large indurated ulcer found about $1\frac{1}{2}$ inches from the pylorus. Posterior gastro-enterostomy	R.	Dr. Tyrie, Keighley. Has "gone on splendidly," August, 1902.	
E. W. Dec., 1901	F.	19	Has complained of pain after food, and vomiting for 16 months. Hematemesis at the onset, but only on two occasions in last 12 months. Pain comes on almost immediately after food. Vomits at least every week. Pain is at once relieved if she lies on the abdomen, prone. Dilated stomach. Free HCl	No ulcer on anterior surface. On posterior surface a large indurated scar. The posterior surface of the stomach was very adherent to the upper layer of transverse mesocolon, the lesser sac being partly obliterated. Posterior gastro-enterostomy	R.	Dr. Tyrie, Keighley. Had a sharp attack of bronchitis after the operation for three days. In September, 1902, was quite well; eating heartily and had gained about 10 lbs. in weight.	

Name and date.	Sex.	Age.	Symptoms and description.	Condition found ; operation.	Result.	Remarks.
N. G., Jan. 1902	F.	26	For last few months has had pain always after food, coming on immediately, and lasting for 3 or 4 hours. Has therefore limited her diet, and has lost weight. Four weeks ago had hematemesis and melena. The melena has continued ever since, and is now threatening to end disastrously. Has fainted in bed several times. Pulse 96; she is very pallid, and has become much thinner during the last 4 weeks	An ulcer in stomach on posterior wall. An ulcer, elongated and thickened, in duodenum, feeling like a date; many adhesions. Posterior gastro-enterostomy	R.	Dr. Ellis, Halifax. This patient made a perfect recovery, and in September, 1902, was reported to be in perfect health. She has regained her lost weight and 7 lbs. over.
M. R., Feb. 3rd, 1902	M.	43	Long-standing stomach trouble. Began 20 years ago; pain after food; and vomiting. Has been more or less subject to indigestion, and has carefully limited his diet; vomiting from time to time in large quantities. Motions occasionally tarry. Last October a sharp attack of hematemesis and melena. Stomach now very dilated, 2 inches below umbilicus. In last 4 months has lost a stone in weight	Very large flaccid stomach. At the pylorus and a little beyond much thickening, forming a tumour equal in size to a walnut. On anterior surface a distinct scar about 3 inches from pylorus. On posterior surface a similar scar with adhesions to transverse mesocolon. Posterior gastro-enterostomy	R.	Dr. Ellis, Halifax. In August, 1902, heard that he was in good health, quite free from stomach troubles, and had gained a stone in weight.
S. H., March 17th, 1902	F.	34	Has suffered intermittently with indigestion since she was 13 years old. For the last 6 years she has been worse, and for the last 2 years she has "not had a bite of solid food," living on milk and milk and soda. Vomiting of blood 6 years ago; neither before nor since. Now vomits large quantities, and says her stomach "seems to fill up for 2 or 3	An enormous stomach. The pyloric antrum is covered with cicatrices, forming an almost continuous fibrous mass. Posterior gastro-enterostomy	R.	Dr. B. W. Hogarth, Morecambe. Weight before operation 5 st. 7 lbs. Never vomited once after operation; was taking solid food when she returned home on seventeenth day. Dr. Hogarth writes in May, "she is enjoying better health than

ever before." May 28th. — Weight, 6 st. 7½ lbs. September, 1902. — "I have been doing 17 or 18 hours work a day, and my work has not been a burden to me, as it was before the operation." Weight 6 st. 10½ lbs.

Dr. Sproule, Mirfield.

R.

A very large flabby stomach. On the anterior surface near the pylorus an ulcer about 1½ inches long by ½ inch wide, very thick and indurated. Posterior gastro-enterostomy

days, and then has to be emptied." Weight 5 st. 7 lbs. Very large stomach on distension, reaches to within 1 inch of umbilicus. Free HCl

F. 25

M. N.,  
April  
17th,  
1901

For several years has suffered from chronic indigestion. Symptoms date from a sudden attack of vomiting with blood-stained ejection. Pain about ½ hour after food; body becomes very distended, belching is frequent, and vomiting occasional. Latter always gives relief. During last June symptoms much worse. Constant indigestion, vomiting, and wasting. Stomach reaches before distension 1½ inches below the umbilicus. Symptoms of ulcer of the stomach 15 years ago. In bed for 6 weeks; pain, hæmatemesis, and wasting. Ever since has had chronic indigestion, never able to eat a hearty meal, solid food causes distension, pain, and vomiting. Now vomits about twice a week, and has measured the amount on two occasions recently, on each 5 pints. Very dilated stomach, splashing and contracting

M. 38

A. W.,  
April  
2nd,  
1902

Dilated stomach. On the posterior surface of the stomach the scar of a large chronic ulcer, with many adhesions to it from transverse mesocolon. Ulcer about 3 to 4 inches from the pylorus, some adhesions also at the pylorus. Posterior gastro-enterostomy

Dr. F. W. Halliday. This patient vomited 1 pint of altered blood on four occasions in first 24 hours after operation. Weight June 18th, 8 st. 7 lbs. August 13th. — 8 st. 8½ lbs. September 13th. — 8 st. 10½ lbs. Had some regurgitant vomiting about twice weekly after the operation; was then ordered to wash the stomach out twice weekly; since then has not vomited. He can eat heartily, has a good appetite, and enjoys his food.

R.

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
M. F., April 17th, 1902	F.	29	From childhood has had trouble with the stomach. Constant indigestion. Four years ago a severe prostrating attack in which she vomited frequently, and blood came on several occasions in large quantities. Indigestion very much worse since that attack—constant regurgitation. In early December last year a similar attack called "gastric ulcer" by Dr. Smith; she was in bed 3 months. Since getting up has had intolerable pain, constant vomiting, and has wasted considerably. Stomach dilated and very tender over pyloric area. Free HCl in excess	Large stomach. Ulcer on anterior wall near the pylorus as large as a shilling, thick and very hard. Adhesions of great omentum to it. Posterior gastro-enterostomy	R.	Dr. Smith, Hunslet. Made an excellent recovery. By September had gained 11½ lbs. in weight, and was free from any discomforts.
M. R., June 4th, 1902	F.	27	Five years ago had an acute attack of abdominal pain, vomiting, etc.; was in bed 22 weeks. The doctor who saw her and the consultant diagnosed "perforating ulcer" of the stomach. Constant indigestion, pain, and vomiting since then; can never take solid food, and ordinary liquid diet causes pain and uneasiness. Vomits every 3 or 4 days now. Stomach moderately dilated	Very dense and numerous adhesions on posterior surface of the stomach, especially thick and tough near the pylorus. A fairly large stomach. Posterior gastro-enterostomy	R.	Drs. Millhouse and Anning. Made a very good recovery.
M. A., June 12th 1902	F.	37	About 10 years ago began with pain and sickness. She was laid up in bed on several occasions. The vomiting was "dreadful," but no blood was ever observed. For 7 years continual indigestion. At the end of that period alarming hemorrhage;	Numerous adhesions at the pylorus and duodenum, especially on the posterior surface. A very large stomach. Some marked local thickening of the head of the pancreas. Posterior gas-	R.	Dr. Ellis, Halifax. By August had gained 12½ lbs. By September 4 additional pounds.

<p>M. G., July 2nd, 1902</p>	<p>M. 47</p> <p>was in hospital 5 weeks. Vomiting and pain have continued intermittently since. Was advised by consultant to undergo operation last year. Dilated stomach. For several months has noticed occasionally that stools "were black as ink."</p> <p>Has had indigestion for 4 or 5 years, gradually increasing in severity until the present time, when he is disabled from work. Pain after food was the first symptom, coming on about 14 hours after a meal, and increasing in severity for an hour unless eased by vomiting, which always afforded relief. There has never been hemorrhage. On examination a very large stomach, descending about 14 inches below umbilicus, before inflation. A few contractions seen on inflation. Has "cramps" in his arms and hands, rarely in his legs; especially noticed during the last 2 months. Tetany</p>	<p>R.</p> <p>A very large stomach. A large scar on the posterior surface near the lesser curvature, about 2 inches from the pylorus. A second scar at beginning of the second portion of the duodenum. Many adhesions round pylorus. Posterior gastro-enterostomy</p>	<p>R.</p> <p>Dr. A. A. McNab.</p>
<p>M. H., July 19th, 1902</p>	<p>M. 30</p> <p>Illness dates from 4 years ago, when he had an attack of hematemesis, bringing up about a pint of blood. He was kept in bed about a month, and apparently made a complete recovery. A year later he developed symptoms of dyspepsia, there being vomiting, especially at night; there was no further hematemesis. Under treatment he improved considerably. 18 months later the same symptoms reappeared, and have remained since, gradually increasing in severity. He now vomits 2 or 3 times a week in very large quantities. The stomach reaches to the pubes, and can be seen actively contracting. He is very thin and much wasted and shrunken. He has not been able to eat solid food for months. Free HCl found on 3 occasions; no lactic acid</p>	<p>R.</p> <p>An enormous stomach, thickly hypertrophied. Dense scarring at and near the pylorus. A few external adhesions. Posterior gastro-enterostomy. This was quite the thickest stomach wall I have seen, and it would be approximately <math>\frac{3}{4}</math> of an inch thick, the increase being due largely to hypertrophy of muscle</p>	<p>R.</p> <p>Dr. Woodratt, Halifax. Weight before, 6st. 10½ lbs. Weight 4 weeks after operation, 7st. 5½ lbs. He could then eat heartily and take any solid food.</p>

Name and date.	Sex. Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
M. W. July 19th, 1902. [H]	F. 24	For 15 months has had symptoms of gastric ulcer, pain, vomiting and inability to take solid food. 11 weeks ago the symptoms became pronounced. Vomiting became frequent. During the last 5 weeks has vomited daily, and on almost all occasions blood has come. While waiting in hospital she vomited 3 times in 5 days, and on each occasion almost half a pint of blood came away	Stomach moderately dilated. On the anterior surface near the pylorus were two scars equal in size to a threepenny piece, distant about 1 inch from each other. A few thin adhesions between these and the anterior abdominal wall. On the posterior surface near the pylorus an indurated area about 1 inch in diameter, with reddened area around it, and covered by recent lymph was found. Several adhesions to the transverse mesocolon. Posterior gastro-enterostomy	B.	Dr. Eskrigge, Royston. An excellent recovery. Vomited once after operation, on 8th day; about 4 ozs. of bile, no blood. In September had gained 8 lbs. in weight, and was eating well.
M. C. July 21st, 1902	F. 35	When 18 to 20 years of age, suffered severely from chlorosis. Four years ago she fell from a ladder, striking the upper part of the abdomen. She was in bed for a fortnight, and suffered great pain and swelling in the upper part of the abdomen. Since this time has had pains after food, fullness and feeling of tight distension, vomiting, and loss of weight. On examination a large dilated stomach, reaching a little below the mid point between umbilicus and pubes. An example of gastric ulcer due to traumatism	A web of adhesions round the pyloric end of the stomach and posteriorly, densest near the pylorus on the posterior surface. A very large, flabby stomach. Posterior gastro-enterostomy	R.	Sent by Dr. Hearder, Ilkley. Weight before operation, 7 st. $\frac{1}{2}$ lb. Weight 3 weeks later, 7 st. 8 lbs.



E. W., July 29th, 1902	F.	32	Symptoms have lasted one year. First noticed discomfort after food, and later acute pain, always in the pit of the stomach. Vomiting set in early, and was frequent. Blood was observed on several occasions; the most vomited at one time was "about a teaspoonful." Latterly has had to limit her diet solely to fluids. On examination a tumour as large as a cocoa-nut found over the pylorus, slightly movable during respiration, a little tender. The stomach is very much dilated. Free HCl always present	A large tumour at the pylorus, and many adhesions to liver, abdominal wall, and pancreas. All perfectly smooth and "finished off." No irregular nodules anywhere. I believed the mass to be inflammatory, and performed gastro-enterostomy	R.	Dr. Baxter Tyrie, August 2nd, 6 st.; August 22nd, 6 st. 7 lbs. Appetite quickly increased, and food was taken freely and without discomfort
J. H., Aug. 7th, 1902	M.	31	Ten months' history of pain after food and gradual loss of weight. All solid food has been abandoned little by little, and now a fluid diet causes pain, occasional vomiting in large quantity, and distension. Had twice had hæmatemesia. The pain is frequently felt about 1½ hours after food. He has lost exactly 4 st. in the last 19 weeks. A very dilated stomach. Free HCl present	While lying under the anæsthetic on the table the dilated stomach showed prominently. It descended a hand's breadth below the umbilicus. On opening the abdomen a thickening of the duodenum above the bile-papilla was felt; the first portion of the duodenum and the stomach were very markedly dilated. Posterior gastro-enterostomy	R.	Dr. Norman Porritt, Huddersfield.

TABLE II (continued).—*Diagnosis: Chronic Gastric Ulcers; Dilated Stomach; Posterior Gastro-enterostomy.*

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
W. D., Aug. 9th, 1902	M.	52	Patient has suffered from indigestion, biliousness, and discomfort after food for 25 years, when he had typhoid fever. Vomiting first occurred 5 years later, was at first infrequent and slight, but later became more frequent and copious. Eight years ago his condition became worse. He had constant severe pain after food, frequent vomiting, often twice daily, and lost over a stone in weight in about 3 months. He improved a little during the following year, but has since steadily lost health and strength. Six months ago was seen by an eminent physician, who diagnosed "cancer of the stomach." His loss of flesh has latterly been extreme—he is now very sallow, wasted, and feeble. The stomach reaches midway between umbilicus and pubes, and can be seen contracting on distension. Free HCl present	A very dilated and somewhat hypertrophied stomach. The scars of 2 large ulcers found on the posterior surface near the pylorus. Adhesion to the transverse mesocolon. Posterior gastro-enterostomy	D.	Dr. Eskridge, Royston. This patient went on very well for 6 days. No vomiting, food taken well and enjoyed, and pulse and temperature were normal. On the seventh day he vomited a little bile. On the eighth he again vomited on several occasions, the pulse rose to 112, and he became slightly jaundiced. He continued to vomit bile in large quantity, though able to take fluid food freely. No food came back in the vomit, only pure bile. As his condition was getting steadily worse I re-opened the abdomen on the fifteenth day, and found gangrene of the gall-bladder. The whole gall-bladder was vivid purplish-green in colour, with greyish patches. Bile had escaped through a sloughing ulceration into the free peritoneal cavity. I cut away a portion of the gall-bladder, and put in drainage-tubes threaded with iodoform gauze. The patient hovered between life and death until Sept. 7th, when he died. At the post-mortem examination no cause for the gangrene was discovered. There was no stone, and the cystic duct, though very tortuous and thickened, was patent. A thick mass was found between the pylorus and pancreas, and many adhesions between these and the transverse mesocolon (?malignant).
C. W., Aug. 23rd, 1902	M.	23	Has suffered from indigestion for nearly 4 years; pain and vomiting almost daily. Has never noticed any blood. Now vomits once or twice weekly in large quantity. A very dilated stomach. On inflation it descends 3½ inches below the umbilicus. Free HCl; no lactic acid	Adhesions between anterior wall of stomach and parietal peritoneum. On separating these a scarring of the stomach wall. A very large stomach. Posterior gastro-enterostomy	E.	Dr. Readman, Skipton.

W. L., Aug. 28th, 1902	M. 19	For 18 months has suffered from indigestion, which, in spite of temporary improvement for a week or two under treatment has steadily got worse. He saw me 4 months ago, and I advised lavage and medicinal treatment, but no benefit has resulted. His diet is now almost entirely liquid, causes him incessant pain; and every week or so he vomits copiously. A very large splashy stomach. Has slight tetanic contractions of hands. Free HCl	A large stomach. On the posterior surface many and thick adhesions, especially near the pylorus. Posterior gastro-enterostomy	R.	Dr. Waugh, Skipton.
J. W. R., Aug. 28th, 1902	M. 46	Symptoms date from last December. Pain over ensiform cartilage, and vomiting. The vomiting was first and chiefly noticed after he had been in bed an hour or two. He had occasionally to get up 3 or 4 times. At Easter the vomiting became more copious, but less frequent. Occasionally "dark brown, with a very bad smell." The stomach is very prominent, standing out boldly from the rest of abdomen, and is actively contracting. Free HCl	The most hypertrophied stomach I have seen. The whole wall at least $\frac{1}{2}$ inch in thickness. A thick, hard ring at the pylorus, and many adhesions. Posterior gastro-enterostomy	R.	Transferred from Dr. Chadwick.
A. S., Aug. 28th, 1902	M. 27	For 2½ years has had "dyspepsia." Complains chiefly of pain on the right side over the pylorus, which begins 2 hours after a meal and gradually increases. He feels "as if he wanted to vomit and can't." Belches sour and offensive gas at intervals. Has severe cramps in muscles of arms, back, and occasionally legs. Lives entirely on milk. Stomach dilated to 1½ inches below umbilicus. Free HCl in excess	A scar near the pylorus about the size of a sixpence. A few adhesions to this and immediately beyond. Similar adhesions on the posterior surface. Posterior gastro-enterostomy	R.	Dr. I. Taylor.

TABLE II (continued).—*Diagnosis: Duodenal Ulcer; Melena; Gastro-enterostomy.*

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
M. P., Sept. 4th, 1902	M.	29	He has suffered for several years from a "weak stomach," having pain after food, 2 or 3 hours after, and occasionally vomiting. Was in his usual state of health up till August 31st last. On that day he had a long and tiring bicycle ride, which left him weary. On Sunday ate heavily and had much discomfort. On Sunday night he got out of bed owing to the feeling of fullness in the stomach and the great uneasiness. He induced vomiting, and the bowels were then moved. He felt faint and cold. On Monday was feeling very tired, so did not get up; still ill and weakly on Wednesday. The stools on both days were quite black. On Wednesday he fainted once while in bed, and felt very chilled. On Thursday the bowels were opened four times, and large tarry stools passed. On Tuesday he was noticed to be very pale; his pallor increased on Wednesday very decidedly. On Thursday morning was seriously ill. Pulse 122, very blanched, felt "dead tired," and the bowels were moving frequently, and on all occasions blood was coming. When I saw him he looked desperately ill. His face and mucous membrane of the mouth blanched to the last degree	We diagnosed chronic duodenal ulcer, with acute deepening and the opening of some large vessel. Operation was advised as a last resort. On opening the abdomen the stomach was found very dilated and full of gas; it contained no blood. The first portion of the duodenum was also dilated. About 1 inch from the pylorus a dense hard mass equal in size to a walnut was felt adherent to the pancreas. Excision of this ulcer was impossible, and therefore gastro-enterostomy was performed. The jejunum at the point opened contained brownish altered blood. The transverse colon was a most vivid dark blue in colour and full of blood	R.	Dr. Fearnley, Harrogate. This patient was in a most critical condition. I have never seen any patient, even after a severe accident, so blanched. While being lifted on to the operation table he complained of being tired and cold, and then fainted.

Miss B., Sept. 16th, 1902	37	<p>Has had indigestion for "many years." Eighteen months ago she had "perforated gastric ulcer" of the sub-acute type diagnosed by Dr. Biahop. Since then her stomach symptoms have been intolerable. Pain constant and gravely increased by food of any kind; vomiting at least every other day, fermentation, and eructation of obnoxious gas. She has vomited frequently half a chamber utensil full of sour semi-digested food. She has "lost a lot of flesh." The stomach is very large, obviously standing out on her thin abdomen. The washing out required 40 pints before the fluid returned clean. Free HCl</p>	R.	<p>The stomach was buried in adhesions to both anterior and posterior surfaces. The whole outline of the stomach was warped. The posterior surface was exposed with some little difficulty owing to adhesions to transverse mesocolon. Posterior gastro-enterostomy was done. I was dissatisfied with the way in which the anastomosis seemed to "sit" after returning within abdomen. Reflux vomiting occurred, 132 ounces of deeply bile-stained fluid were vomited in two days. I therefore reopened the abdomen, and performed an entero-anastomosis between the afferent and efferent limits of the anastomosing loop</p>	Dr. R. W. S. Biahop, Kirby Malzeard.
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TABLE II (continued).—*Diagnosis: Chronic Gastric Ulcer; Posterior Gastro-enterostomy.*

Name and date.	Sex.	Age.	Symptoms and description.	Condition found; operation.	Result.	Remarks.
Miss T., Sept. 25th, 1902	F.	28	Has had stomach trouble since she was 15. "Attacks" of pain, vomiting, and inability to take food, lasting 2 to 3 weeks. Then for a week or two she is much better, until another "attack" commences. Has had continuous medical treatment without lasting benefit. During the last 6 or 8 months her pain has been constant, a "dull ache," increased by food, and eased by vomiting. Has not been able to take an ordinary meal for at least 6 months. There is marked epigastric tenderness Has been in failing health for 9 to 10 months. The chief symptom has been vomiting. At the onset a sudden seizure of vomiting, very acute and lasting over 24 hours. There has been a series of attacks of vomiting. Pain is noticed about an hour before a meal is due, and lasts from a few minutes to 2 or 3 hours; is never very severe. She has lost flesh, and has got weaker, occasionally having to spend a part of the day in bed. No melæna. No hæmatemesis. A small hard tumour felt above, and to the right of the umbilicus, a little movable. On distension with CO <sub>2</sub> an enormous stomach, reaching a full hand's breadth below the umbilicus	A large stomach. Along the lesser curvature, near the middle of the stomach is a broad indurated band about 2 inches in length, and 1 inch in breadth. On the posterior surface this is felt and seen more clearly than on the anterior, and a few adhesions are found. Posterior gastro-enterostomy	R.	Dr. O'Connell, Keighley.
Mrs. B., Feb. 25th, 1902, Stanningley	F.	60	On examination the stomach is just down to the umbilicus. on firm pressure. Free HCl. Never hæmatemesis	A very large stomach. On posterior surface of the stomach one large ulcer with several thick adhesions around it. In the second portion of the duodenum the tumour is found. It is a mass about the size of a large walnut, adherent to the pancreas, with which it seems inseparably connected. The duodenum above this point looks distended. Probably chronic duodenal ulcer with interstitial pancreatitis	R.	Dr. Welch, Stanningley.

## DISCUSSION

Mr. D'ARCY POWER said that by the kindness of Mr. Willett he had operated, at St. Bartholomew's Hospital, on a good many cases of acutely perforating ulcers of the stomach and duodenum. From the delay which occurred before the cases came under his care he was inclined to think that many practitioners were still in the position they used to maintain in regard to hernia and intussusception, viz. disposed to postpone operation because some cases recovered spontaneously. Mr. Power held very strongly that not only should an operation be performed at the earliest opportunity in all cases where perforation had obviously occurred, but that the abdomen should be opened when there was even a suspicion of perforation. He asked Mr. Moynihan what attitude he held towards drainage after operation and suture of a perforating ulcer. For his own part, he had good and bad results alike after immediate closure of the abdominal wall and after the most free drainage, the usual abscess being subphrenic in position. Mr. Power also referred to the confusion which sometimes, and apparently necessarily, occurred in the diagnosis of the rarer perforated duodenal ulcer with the more common appendicitis. He attributed the excellent recovery which followed in one of his cases where this mistake had occurred to the very free abdominal opening which he was obliged to make to correct his error. He also asked for details as to feeding after operation, for his experience had taught him that much trouble arose from over-feeding in these cases, though the patients fortunately gave timely warning by vomiting.

He quite approved of the abandonment of pyloroplasty, and thought that the method of direct suture was certainly the most satisfactory way of performing gastro-enterostomy, though in one case he had obtained a very satisfactory result from the use of McGraw's elastic ligature. It did not appear, however, that this method had any particular advantage over direct union. There had been very little vomiting in the cases of gastro-jejunostomy whose course he had followed after operation, and he was fully in agreement with Mr. Moynihan that the "vicious circle," which was so great a bugbear in this operation, was due to a defective apposition of the intestine to the stomach, which allowed of tension or traction on the parts.

The PRESIDENT (Mr. Alfred Willett) said the paper dealt with two groups of cases, perforating gastric and duodenal ulcer being the first. In regard to this, there was a consensus of opinion amongst surgeons that the more quickly a diagnosis was made and an operation performed the better the chances of success.

The second group comprised the cases, nearly fifty in number, of chronic dyspepsia due to the causes enumerated. The success which had attended operations in this latter group was very great for not only was the immediate result good, but the subsequent results were most satisfactory, for the patients were rescued from a condition of chronic invalidism. In the tabulated cases the accuracy of diagnosis was remarkable. In not one of the cases recorded had the abdomen been opened without finding some lesion. Another point was the evident futility of drug treatment in such conditions as the author had found. It was a striking result that in nearly fifty cases there was only one death. In nearly every instance the immediate benefit was very great, and in nearly all the ultimate result was good. Simplicity in the technique of all such operations was the great aim, and in the operation described in the paper the manipulations were as simple as could well be imagined.

Mr. T. C. ENGLISH referred to forty consecutive cases of perforated gastric and duodenal ulcer which had been operated on in St. George's Hospital. Of these, twenty-one recovered. Many illustrated the latency of symptoms in the reaction stage. Details were given of some such cases. Of other cases which resembled perforated gastric ulcer in which exploratory operation was indicated, but in which no ulcer had been found, many were associated with the catamenia in neurotic women.

Mr. PERCY PATON referred to the observations in the paper on the slight importance of drainage, and asked what was the objection to local drainage. He considered that it tended to prevent the formation of local abscess in the vicinity of the perforation, though it might not be successful in doing so, while at the same time it did no harm.

Dr. NEWTON PITT, in regard to the alleged absence of anæmia in acute ulcer, said that this was not borne out in his experience. In a certain number of acute cases there was profound anæmia. He asked, was there any post-mortem evidence that hard chronic ulcers did heal after a gastro-enterostomy? Chronic ulcers, though often multiple, were, he thought, more usually single.

Mr. MOYNIHAN, in reply, thought that if there were the smallest doubt of perforation the abdomen should be opened. As a matter of fact, he had never opened the abdomen without finding a perforated gastric or duodenal ulcer. Allusion was made to three successive cases in one hospital, in which operation had been performed without finding any perforation. Drainage was of much less importance than the possibility of getting the peritoneum clean. In one case not drained there was subphrenic abscess. If the peritoneum could be cleansed drainage was unnecessary. He had drained three cases out of eleven. Much in regard to feeding depended on the patient; many cases he had seen in the early days had been lost from starvation. The



principle should be to give fluids as early and in as large quantity as possible. He had had no special experience of the elastic ligature. He did not intend ever to use a Murphy's button again. It was important to use the method of suture with which the operator had the greatest familiarity. From his comparatively small experience he would say that if there were anæmia after acute ulcer it was transient; in chronic ulcer it persisted for months. He had never had the chance of verifying the cure of chronic gastric ulcer post mortem, but complete recovery of health from an apparently moribund condition due to chronic ulcer followed gastro-enterostomy. In regard to the multiplicity of ulcers, he felt sure that chronic ulcers were never solitary. He did not believe that a duodenal ulcer often occurred without a gastric ulcer.



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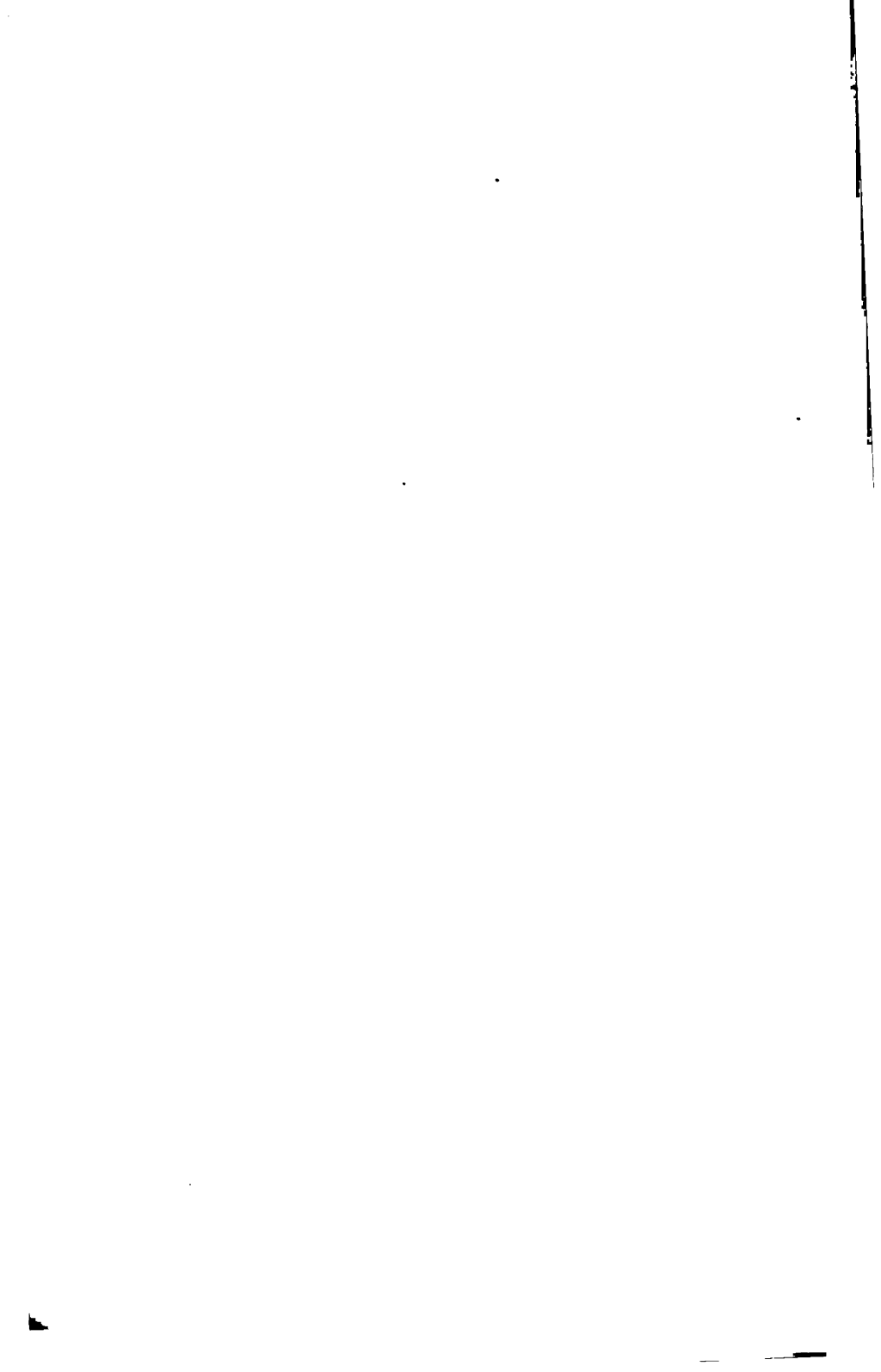
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CHARTER AND BYE-LAWS  
OF  
THE ROYAL  
MEDICAL AND CHIRURGICAL SOCIETY  
OF  
LONDON.



LONDON:  
1903.





# CHARTER

AND THE

## BYE-LAWS,

AS APPROVED AND CONFIRMED BY SPECIAL GENERAL  
MEETINGS, JUNE 8TH, 1897, JUNE 12TH, 1900, AND  
MARCH 1ST, 1902.



## CHARTER.

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WILLIAM THE FOURTH, by the Grace of God of the United Kingdom of Great Britain and Ireland King, Defender of the Faith—To ALL to whom these presents shall come GREETING.

5 WHEREAS John Elliotson Doctor of Physic, Sir Astley Paston Cooper Baronet, and John Yelloly Doctor of Physic have, by their petition, humbly represented unto us that a Society was formed in the year one thousand eight hundred and five, by a considerable number of Physicians and Surgeons of eminence in London, for the cultivation and promotion of Physic and Surgery, and of the branches of Science connected with them, of which the last two named of the petitioners were original members; and that the said Society has expended considerable sums of money in the purchase and collection of a large and valuable library, and has published eighteen volumes of Transactions which have had a very extensive circulation. AND WHEREAS they, the said petitioners, have humbly besought us that we should give to them and to the other persons who have already become Members of the said Society, or who may at any time hereafter become Members of it, our Royal Charter of Incorporation for imparting greater stability and effect to the designs of the said Society. Now KNOW YE, that we, being desirous of encouraging a design so laudable, have of our special grace, certain knowledge, and mere motion, will, granted and ordained, and Do by these presents for us, our heirs and successors, will, grant and ordain that the said John Elliotson, Sir Astley Paston Cooper, and John

I. Petition for a Charter,  
and grant of it to the present Members and those who shall be elected according to future Bye-laws.

Yelloly, and such others of our loving subjects as are now Members of the said Society, or who shall at any time hereafter become Members thereof, according to such Byelaws as shall hereafter be framed or enacted, shall by virtue of these presents be called Fellows of the said Society, and shall be one body politic and corporate, by the name of *The Royal Medical and Chirurgical Society of London*; of which Society we do hereby declare ourselves, and successors if they shall think fit, the Patron, by which name they shall have perpetual succession, and a common seal with full power to alter, vary, break and renew the same at their discretion, and by the same name to sue and be sued, to implead and be impleaded, to answer and be answered unto in every court of us our heirs and successors, and be for ever able and capable in the law to purchase, receive, hold, possess, and enjoy to them and their successors, any goods and chattels whatsoever, and also be able and capable in the law (notwithstanding the Statutes of Mortmain) to take, purchase, hold and enjoy to them and their successors, any lands, tenements or hereditaments whatsoever, the yearly value of which shall not exceed in the whole the sum of two thousand pounds, computing the same respectively at the rack rent which might have been had or gotten for the same respectively at the time of the purchase or acquisition thereof; and shall have full power and authority to sell, alien, charge or otherwise dispose of any real or personal property so to be by them acquired as aforesaid, and to act and do in all things relating to the said corporation in as ample manner and form as any other our liege subjects, being persons able and capable in the law, or any other body politic and corporate in our said United Kingdom of Great Britain, may or can act or do.

AND WE DO further declare and grant that for the better government of the said Society and for the better management of the concerns thereof, there shall be, from the date of these presents thenceforth and for ever, a President of the said Society, who with twenty Fellows to be elected in

II. Appointment of the first President, and first two Members of Council

manner hereinafter mentioned shall form the Council. And we do hereby appoint the said John Elliotson the first President of the said Society, and the said Sir Astley Paston Cooper and John Yelloly the first Members of the Council,

- 5 to continue in office till the first day of March next. AND who are to be joined within four months by eighteen other Members of Council appointed at a General Meeting: and all to remain in office till the 1st of March.  
 WE FURTHER DIRECT that within four months from the date of these letters patent, a General Meeting of the Fellows of the said Society shall be held, who shall be authorised by method of ballot to elect eighteen fit and proper persons as officers and other Members of the Council, to complete the number of twenty-one, of whom including the President We have willed that the Council shall be composed, and that such additional persons shall likewise continue in office till the first day of March next, and till
- 10 other fit and proper persons be chosen in their room.

- AND OUR further will and pleasure is, that the Fellows of the said Society shall and may on the first day of March one thousand eight hundred and thirty-five, and also shall and may on the first day of March in every succeeding year or as near the same as conveniently may be, assemble together at the then last or other usual place of meeting of the said Society, and proceed by method of ballot to nominate and appoint a President of the said Society, and such Officers and other Members of the Council as may
- 20 with the President form the number of twenty-one, of whom we have willed that the Council shall consist; and also may in case of the death, resignation or removal of the President or any Officer or other Member of the Council within the space of three months next after such death, resignation or removal, elect some other person being a Fellow of the said
- 25 Society to supply the place of such President or Officer or other Member of the Council. And Our further will and pleasure is, that no Fellow who has filled the office of President for two successive years shall be again eligible to the same situation until the expiration of one year from the termination of his office, and that not more than two thirds of the Fellows who have formed the Council of the
- III. The Society to appoint twenty-one Officers and other Member of Council on the 1st of March in every year, to fill up vacancies that may occur in the intervals; not to appoint the same President for more than two successive years, nor ever elect more than two thirds of the

Members of the last Council; to have the power of electing new Fellows, and expelling Fellows. preceding year shall be re-elected Members of the Council at such annual meeting. And we do further grant and declare that the Fellows of the said Society or any ten or more of them shall and may have power from time to time at the meetings of the said Society to be held at the usual place of meeting of the said Society, or at such a place as shall have in that behalf been appointed, by and with the consent of not less than four fifths of the Fellows present, to elect such persons to be Fellows of the said Society, and all Fellows to remove from the said Society, as they shall think fit; and that the Council hereby directed to be appointed and the Council of the said Society for the time being, or any three or more of them, all the members thereof having been first duly summoned to attend the meetings thereof, shall and may have power according to the best of their judgment and discretion to make and establish such Bye-laws as they shall deem proper and necessary for regulating the affairs of the said Society, and also the number and description of its Officers, and also the times, place and manner of electing and removing the Fellows of the said Society and all such subordinate servants, officers, and attendants as shall be deemed necessary or useful for the said Society, and also for filling up from time to time any vacancies which may happen by death, resignation, removal, or otherwise in any of the offices or appointments constituted or established for the execution of the business and concerns of the said Society, and for regulating and ascertaining the qualifications of persons to become Fellows of the said Society respectively, and also the sum and sums of money to be paid by them respectively, or any of them, whether upon admission or otherwise, towards carrying on the purposes of the said Society, and also the number, qualifications and privileges of such persons as they may from time to time deem it proper to admit as Honorary Fellows: and such Bye-laws from time to time to vary, alter or revoke and make such new and other Bye-laws as they shall think most useful and expedient. so that the same be

The Council to have the power of making Bye-laws, for regulating the affairs of the Society, the description and number of its officers, elections and expulsions, appointment of subordinate Officers, filling up vacancies, determining the qualifications of candidates, the amount of entrance and subscription money, and the qualifications of Honorary Fellows; and to have the power of altering and revoking such Bye-laws as may be

not repugnant to these presents, or to the laws of this our Realm: PROVIDED, that no Bye-law hereafter to be made, or alteration or repeal of any Bye-law which shall hereafter have been established by the said Council hereby directed

made,—  
Provided  
the Society  
sanction the  
proceeding of  
the Council.

5 to be appointed, shall be considered to have passed and be binding on the said Society, until such Bye-laws or such alteration or repeal of any Bye-laws shall, after such notice to the Fellows as from time to time may be deemed expedient by the said Society, have been confirmed

10 by ballot by the members at large of the said Society, ten at least of the Fellows of the said Society being present: and Provided that no such Bye-law or alteration or repeal of any Bye-law shall be deemed or taken to pass in the affirmative, unless it shall appear upon such ballot that not

15 less than two thirds of the Fellows present at such meeting shall have voted for the same. And Our further will and pleasure is, that it shall be lawful for any three

Fellows, by writing under their hands transmitted to the President or such other officer or officers as may by the

Any three  
Fellows may  
make recom-  
mendations  
respecting  
Bye-laws to  
the Council—

20 Bye-laws hereafter to be made be designated for the purpose, to recommend to the Council any new Bye-laws or alteration or repeal of any existing Bye-laws; and in case the Council shall not agree to such new Bye-laws or alteration or repeal of any existing Bye-laws, then Our

25 will and pleasure is, that such propositions shall, if required by the said three Fellows, be submitted to the consideration of the Society at large, and determined on by them in the same way as has been directed with regard to new Bye-laws or alterations or repeals of

or to the  
Society, if  
the Council  
dissent from  
the recom-  
mendation.

30 existing Bye-laws which have been approved by the Council. IN WITNESS whereof we have caused these Our Letters to be made Patent. WITNESS Ourself, at our Palace at Westminster, this thirtieth day of September, in the fifth year of our reign.

35

By WRIT OF PRIVY SEAL,

EDMUNDS.

# BYE-LAWS.

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## CHAPTER I.

### *Of the Object and Constitution of the Society.*

- Object of the Society.** 1.—THE ROYAL MEDICAL AND CHIRURGICAL SOCIETY is instituted for the cultivation and promotion of Medicine 5 and Surgery, and the branches of Science connected therewith.
- Number of Honorary Fellows.** 2.—The Society shall consist of Fellows and Honorary Fellows. The Fellows shall be unlimited in number; the Honorary Fellows shall not exceed twelve British sub-10 jects, and twenty Foreigners.
- Radius of Resident Fellowship.** 3.—Such of the Fellows as reside within seven miles of the Society's House shall be considered as Resident Fellows: all the others as Non-resident.
- Of whom Fellows may consist.** 4.—The Fellowship of the Society shall be restricted 15 to men, who are registered medical practitioners of the United Kingdom and to others whose qualifications are satisfactory to the Council.
- Honorary Fellows—British** 5.—British subjects who have eminently distinguished themselves in Medicine, Surgery, or in Sciences con-20 nected therewith, but are not engaged in practice, shall be eligible as Honorary Fellows.
- and Foreign.** 6.—Foreigners who have eminently distinguished themselves in Medicine, Surgery, or in Sciences connected therewith, shall be eligible as Honorary Fellows. 25
- Officers and Council.** 7.—The Officers of the Society shall be elected from the Fellows, and shall consist of a President, four Vice-



Presidents, two Treasurers, two Secretaries, and two Librarians, who together with as many other Fellows as shall make up twenty-one, shall constitute the Council, and shall have the management of the Society's affairs.

## 5

## CHAPTER II.

*Of the Election and Admission of Fellows.*

1.—EVERY Candidate for admission into the Society as <sup>Proposal of</sup> a Fellow shall be proposed and recommended by three or <sup>Candidates</sup> more Fellows, who shall deliver a paper signed by them- <sup>for</sup> Fellowship.  
 10 selves to one of the Secretaries, specifying the full name of such person, his professional qualifications and whence obtained, together with his department of practice and usual place of residence, and that he is a fit and proper person to be elected a Fellow; all which shall be certified  
 15 from their personal acquaintance with him. But, if such Candidate be resident abroad, such proposal and recommendation from one Fellow shall at the discretion of the Council be sufficient, together with a recommendation signed by two other Fellows, certifying, from their know-  
 20 ledge of his works, that he is a fit and proper person to be elected a Fellow. Every recommendation shall be <sup>Recommendations to be</sup> suspended in the Library of the Society for one meeting <sup>suspended in</sup> at least, exclusive of that on which it was presented, and <sup>the Library.</sup> shall remain suspended until the ballot for election shall  
 25 take place.

2.—A list shall be sent to each Resident Fellow <sup>List of</sup> fourteen days before the day of election, containing the <sup>Candidates to</sup> name of every Candidate whose recommendation has been <sup>be sent to</sup> suspended in accordance with the preceding law; and <sup>Resident</sup>  
 30 such list shall specify the full name of such person, his professional qualifications and whence obtained, together with his department of practice and usual place of resi-

Election by  
ballot.

Votes  
necessary to  
secure  
election.

When  
elections take  
place.

dence, and also the names of the Fellows who have recommended him to the Society for election. The election of Fellows into the Society shall be by ballot, and the ballot shall be taken in such manner as the Council shall from time to time determine; and no person shall be declared elected unless he have in his favour the votes of four fifths of the Fellows voting, ten Fellows at the least voting. The election of Fellows shall take place on the first Ordinary General Meetings of the Society in December, February, April, and June, and the ballot shall be taken in the presence of not less than two Members of the Council, and the result shall be declared by the President or Fellow presiding.

Appearing for  
admission.

3.—Every person elected a Fellow of the Society shall, if he live within seven miles of the Society's House, have immediate notice of his election sent to him in such form as the Council may from time to time direct, and shall appear for his admission on or before the fourth Ordinary Meeting of the Society after his election, or within such further time as shall be granted by the Council; otherwise his election shall be void.

Obligation to  
be subscribed  
by Fellows.

4.—Such person shall previously to his admission, subscribe the following Obligation in the Obligation Book:

“We, whose names are hereunto subscribed, having been elected Fellows of the Royal Medical and Chirurgical Society of London, hereby promise, that we will, so long as we shall be and continue Fellows, to the utmost of our power, promote the honour and interest of the said Society, and observe the enactments of its Charter and Bye-Laws.”

30

Form of  
admission for  
Resident  
Fellows.

If any person elected shall refuse to subscribe this Obligation, his election shall be void.

5.—The admission of any Fellow into the Society shall be at some meeting thereof, in manner and form following, he having first paid the Admission Fee and subscribed the Obligation; viz. being presented by some Fellow, the President, or Fellow officiating in his stead,

35

shall address him in these words :—"By the authority and in the name of the Royal Medical and Chirurgical Society of London, I admit you a Fellow thereof."

- 6.—Such persons as may be elected Fellows of the <sup>Form of</sup> Society, and do not live within seven miles of the Society's <sup>admission for</sup> House, shall have immediate notice of their election sent <sup>Non-Resident</sup> to them, in such form as the Council may from time to time direct, together with an Obligation form, and shall be considered Fellows on paying the Admission Fee and <sup>Fellows.</sup> returning the Obligation duly signed on or before the fourth ordinary Meeting of the Society after their Election, or within such further time as shall be granted by the Council, otherwise their election shall be void.

- Medical Officers of the Navy, Army, and Indian Medical <sup>Service</sup> Services, on active service, shall be admitted to the <sup>Fellows.</sup> Society on the same terms as Non-resident Fellows, but no annual contribution shall be required for any complete Society's year passed outside the United Kingdom, provided that due notice has been given to the Society. In the case of Service Fellows the Council shall be empowered to accept the nomination paper of a candidate who is supported by only one Fellow from personal knowledge, provided that at least two other Fellows, who shall be Members of Council, shall subscribe their names.

- 7.—The election, or re-election, of every person <sup>Elections and</sup> into the Society, with the time thereof, shall be recorded <sup>re-elections to</sup> in a book to be kept for that purpose; but if it appear <sup>be recorded in</sup> upon the ballot that the person proposed is not elected or re-elected a Fellow, no notice of the decision shall be taken in the minutes.

### CHAPTER III.

#### *Of the Election of Honorary Fellows.*

- 1.—THE power to recommend persons as Honorary <sup>Recommendation and</sup> Fellows shall be vested in the Council, and their election <sup>election of</sup> shall be conducted in the same manner as that of other <sup>Honorary</sup> Fellows.

Fellows, with the exception that personal acquaintance shall not be necessary in recommending them.

Form of  
admission for  
Honorary  
Fellows.

2.—Honorary Fellows shall have a Diploma, in such form as the Council may from time to time direct, transmitted to them; and when present at a General Meeting 5 of the Society, shall be admitted with formalities similar to those prescribed for the admission of Fellows.

Privileges of  
Honorary  
Fellows.

3.—The Honorary Fellows shall enjoy the privilege of attending and introducing friends at the Ordinary General Meetings of the Society, and when Resident, of 10 using the Library in the same manner as ordinary Fellows, but shall not be entitled to any further privileges, without special leave, granted by the Society, at the recommendation of the Council.

#### CHAPTER IV.

15

##### *Of the Withdrawing and Removal of Fellows.*

Withdrawing  
of Fellows.

1.—ANY Fellow may withdraw from the Society, upon signifying his desire to do so, by letter addressed to the Secretaries; provided he shall have paid whatever may be due from him to the Society, and shall have returned 20 all books in his possession belonging to the Society.

Removal of  
Fellows.

2.—Whenever there shall appear cause, in the opinion of the Council, for the removal of any Fellow from the Society, a minute shall be made thereof, and a copy of such minute forthwith sent to the Fellow, and a special 25 meeting of the Council summoned thereupon, which the Fellow, whose conduct is in question, shall be invited to attend. If after investigation, the Council shall still consider the removal of such Fellow advisable, they shall frame a resolution to that effect, which shall be suspended in the 30 Society's Library for at least fourteen days, and be submitted to a Special General Meeting of the Society. On the resolution being put to the ballot, and four fifths of the Fellows present voting for it (ten at the least being present), the President or Fellow presiding shall declare 35 such Fellow removed from the Society accordingly.

## CHAPTER V.

*Of the Contributions of Fellows.*

- 1.—EVERY person elected a Fellow of the Society, and Admission Fee for Resident Fellows. living within seven miles of the Society's House, shall, previously to his admission, pay to the Society the sum of Six Guineas as an Admission Fee, which sum shall not be held to include an annual contribution; and shall afterwards contribute the sum of Three Guineas annually. But every Annual Contribution of ditto. Fellow may, after the payment of the Admission Fee, Compounding for the Annual Contribution. compound for his annual contribution by paying at one time the sum of Fifty Guineas. Every Fellow who has paid five or more annual contributions may compound for all future annual contributions, by paying at one time the sum of Forty-five Guineas; every Fellow who has paid ten or more annual contributions may compound for all future annual contributions by paying at one time the sum of Thirty-nine Guineas; every Fellow who has paid fifteen or more annual contributions may compound for all future annual contributions by paying at one time the sum of Thirty-two Guineas; every Fellow who has paid twenty or more annual contributions may compound for all future annual contributions by paying at one time the sum of Twenty-four Guineas; every Fellow who has paid twenty-five or more annual contributions may compound for all future annual contributions by paying at one time the sum of Fifteen Guineas; and every Fellow who has paid thirty or more annual contributions may compound for all future annual contributions by paying at one time the sum of Five Guineas: provided always that no Fellow may compound for future contributions, from whom an annual contribution is, at the time, due.

- 2.—All sums of money paid to the Society as composition fees in lieu of annual contributions shall be applied in How Composition Fees are to be applied.

reducing the principal money owing upon the debenture loan of the Society, and shall be paid by the Treasurers to the Trustees for the debenture holders as and when the Council shall from time to time direct.

When yearly Contributions are payable.

3.—Annual contributions shall be payable at each 5 Annual General Meeting, for the current year; but no Fellow elected within three months preceding the Annual Meeting shall be liable to such contribution till the second Annual General Meeting from the time of his election.

Subscriptions in arrear.

4.—Every Fellow whose annual contribution shall be 10 more than three months in arrear shall have his name suspended in the Society's Library, and shall not enjoy any of the privileges of a Fellow until such annual contribution be paid.

When a Fellow forfeits his Fellowship and how he may be re-elected.

If the said contribution shall not be paid on or before the first meeting in the November following, and 15 no reason be assigned, satisfactory to the President and Council, for such non-payment, he shall cease to be a Fellow of the Society. Provided that on a request in writing for readmission being addressed to the President and Council by an individual so circumstanced within the 20 space of three months following such meeting in November, the case shall be stated by the President from the Chair at one of the ordinary General Meetings of the Society, and the question of his readmission shall be decided by ballot at the next ordinary General Meeting; 25 but no person so applying shall be declared re-elected unless he shall have in his favour the votes of four fifths of the Fellows voting, ten Fellows at the least voting.

Admission Fee for Non-Resident Fellows.

5.—Every person who shall after the 8th day of June, 1897, be elected a Fellow of the Society and does not live 30 within seven miles of the Society's House, shall pay to the Society the sum of Three Guineas as an admission fee, and shall after the first year from his admission (the said admission fee being deemed to include his first year's annual contribution) contribute the sum of One Guinea 35 annually, and shall be entitled to consult Books and Periodicals in the Reading Room, and to borrow one volume at a time

Annual Contribution of ditto.

from the Library. Any Non-resident Fellow wishing to enjoy the full privileges of a Resident Fellow, shall be at liberty to do so on paying an additional Three Guineas as admission fee and the annual contribution of Three Guineas. How Non-Resident Fellows may enjoy the privileges of Resident Fellows.

6.—Any Non-resident Fellow, who shall, by change of residence, become a Resident Fellow, shall subscribe the Obligation, pay an additional Three Guineas as admission fee, and the annual contribution of Three Guineas like 10 other Resident Fellows. Non-Resident Fellows who become Resident.

7.—Any Resident Fellow of the Society, who by change of Residence shall become Non-resident, shall, from the date of the next Annual Meeting, be only liable to pay the annual contribution of a Non-resident Fellow: 15 and the same shall apply to any temporary absence, provided it include the whole period between one Anniversary Meeting and another. Resident Fellows who become Non-Resident.

8.—The determination of what constitutes Residence, or Non-residence, and the adjustment of any payment as 20 a composition fee in lieu of annual contributions, or for the 'Transactions,' which may become necessary when a Resident Fellow becomes Non-resident, or when a Non-resident Fellow becomes Resident, shall be left to the discretion of the Council, as occasion arises.

## CHAPTER VI.

*Of the Election of Officers and Council.*

1.—EVERY Fellow of the Society resident in the United Kingdom shall be summoned to the Annual Meeting, at least a week before the day on which it shall take place, 30 by a letter signed by the President and the Secretaries. Notices of the Annual Meeting sent to Fellows.

2.—All the Members of the Council shall be elected annually by ballot; but no Fellow shall be eligible to the Election of Council and Officers.

Eligibility of  
Fellows for  
Offices.

office of President, Vice-President, or Councillor for more than two years in succession. Neither shall any Fellow be eligible for the office of Treasurer, Secretary, or Librarian, for more than two years in succession, unless recommended for re-election by a majority of not less than two thirds, 5 ascertained by ballot, in a meeting of Council specially summoned for the consideration of the house-list, provided always that not more than two thirds of the Fellows who have formed the Council of the preceding year shall be re-elected Members of the Council at such Annual Meeting. 10

Balloting lists  
for Officers  
and Council.

3.—Balloting lists, recommended by the Council, and having blank spaces for such alterations as any Fellow may wish to make in them, shall be laid on the Society's table, for the use of the Fellows, and sent to each Fellow resident in the United Kingdom, with the circular summons, 15 seven days previously to the day of election.

Ballot at the  
Annual  
Meeting.

4.—The Chair shall be taken at the Annual Meeting at such time as shall be fixed upon by the Council, which time shall be inserted in the circular summons, and the ballot shall continue open for not less than one hour. 20

Scrutineers.

5.—The President, or Fellow presiding in his stead, shall appoint, from the Fellows present, two or more scrutineers, to superintend the ballot in its progress; and when it is closed to examine the lists, and report the result to the President. Each Fellow voting shall place his list, folded, 25 in the ballot box; and the name of each Fellow voting shall be recorded.

In case of  
equality of  
votes, election  
determined by  
President.

6.—If any Fellows have an equal number of votes for an office in the Society, or place in the Council, the person to be elected shall be determined by the President. 30

## CHAPTER VII.

### *Of the President and Vice-Presidents.*

Duties of  
President.

1.—THE President shall preside at all the Meetings, and regulate all the proceedings of the Society and Council.



He shall state and put questions, both in the affirmative and negative, according to the sense and intention of the Meeting ; he shall maintain order in the proceedings, and execute, and see to the execution of the Provisions of the 5 Charter and Bye-Laws of the Society. He shall, after the minutes of each meeting are read over, with the approbation of the Meeting, sign them, as a voucher for their accuracy.

2.—In the absence of the President, the Vice-Presidents 10 in rotation, or, in their absence, one of the Treasurers, or a Fellow chosen by the Fellows present, shall take the Chair, and act in all respects as the President is em-  
Duties of  
Vice-  
Presidents  
other  
Chairman  
 powered to do by the Charter and Bye-Laws of the Society.

## CHAPTER VIII.

15

### *Of the Treasurers.*

1.—THE Treasurers, or some persons appointed by them, shall receive, for the use of the Society, all sums of money due or payable to the Society ; and, out of such money, shall pay and disburse all sums of money which may be due 20 from, or payable by, the Society ; and shall keep particular accounts of all such receipts and payments, in the way which may seem most proper to the Council.

2.—They shall not pay any sum of money on account of the Society without the sanction of the Council, or of a 25 Standing Committee, which has been empowered by the Council to order payments.

3.—All sums of money in the hands of the Treasurers, not immediately required for the use of the Society, shall be invested in such Government or other securities as shall 30 be approved of, and directed by, the Council.

4.—The Treasurers shall keep a book of printed check receipts for annual contributions ; each receipt shall be

signed by both of them, and be filled up with the name of the Fellow paying, the sum paid, and the time for which the contribution is paid. These receipts shall be countersigned by the person who shall receive the money on the Treasurers' behalf, and who, upon the delivery of the receipt to the Fellow paying, shall enter upon the counterpart thereof the above particulars, and the day of payment. The same proceedings shall be observed with regard to the receipts for admission and composition fees.

Accounts to be audited and laid before the Council and the Society.

5.—The accounts of the Treasurers shall be audited annually by a Chartered Accountant to be appointed by the Council. The accounts so audited shall be laid before the Council at their meeting in February, and presented to the Society at the Annual General Meeting.

## CHAPTER IX.

15

### *Of the Honorary Secretaries.*

Duties of Secretaries.

1.—THE Secretaries shall have the management of the correspondence of the Society and Council, except in so far as the Council shall otherwise direct.

2.—The Secretaries shall attend all meetings of the Society and Council, and shall be *ex officio* members of all Committees; when the Chair has been taken, one of them shall read the minutes, orders, and entries of the preceding meeting, and shall take minutes of the business and orders of the meeting; and at the meetings of the Society shall mention the gifts made since the last meeting; shall give notice of candidates that stand proposed for election into the Society; shall read the letters; and shall read the papers presented to the Society, as far as possible, in the order of time in which they were received, unless the President shall otherwise direct.

3.—The Secretaries shall have the charge, under the direction of the Council, of printing the Transactions of the Society, and of correcting the press.

## CHAPTER X.

*Of the Honorary Librarians.*

- 1.—THE Librarians shall have the superintendence of all matters relative to the Library, and be permanent members of the Library Committee. <sup>Duties of Honorary Librarians.</sup>
- 2.—They shall, with the assistance of the Library Committee, inspect the Library once at least in every three years, and make a report on the state of it to the next Annual General Meeting of the Society.
- 3.—They shall, under the direction of the Council, order books, and be responsible for the printing of Catalogues of the Library, and for the entering of titles of all new works in the Catalogues.

## CHAPTER XI.

*Of the Secretary and the Librarian.*

- 1.—THE Secretary shall either not be a Fellow of the Society; or, if a Fellow, shall cease to be so on his election to and acceptance of that Office. <sup>Secretary and his duties.</sup>
- 2.—The Secretary shall give such security as may be required by the Council.
- 3.—The Secretary shall transact the general business of the Society and conduct its correspondence under the direction of the Council and of the House Committee; he shall receive all papers submitted for reading, send them to the appointed referees, enter the referees' reports in the proper book, and pass the Society's publications through the press; he shall supervise the servants of the Society in their work, and be responsible for their orderly conduct; he shall supervise and take care of the Societys'

premises and other property, report on defects, and deal with emergencies; he shall be in attendance during all meetings of the Society, of the Council, and of the House Committee, and shall attend daily at the Society's House for such time as shall be fixed by the Council in the "Standing Orders." He shall further generally assist the Hon. Secretaries in the non-scientific part of their work.

Librarian and  
his duties.

4.—The Librarian shall be responsible for the arranging and cataloguing of the books, and generally for the proper conduct of the Library; he shall attend daily between the 10 hours of 10 a.m. and 6.30 p.m.; he shall be in attendance at the meetings of the Library Committee, and shall submit to the Hon. Librarians and the Library Committee all books recommended to be added to the Library or offered for purchase, and be responsible for the keeping in proper order of the books and other contents of the Library.

## CHAPTER XII.

### *Of the Council.*

Duties of the  
Council.

1.—THE Council shall have the management of the affairs of the Society, and shall appoint such officers and servants as they may deem necessary; shall fix their duties, and suspend or remove them when they see occasion. They shall determine upon such security as may be proper to be given by such officers and servants.

Meetings of  
Council.

2.—The Council shall meet at the House of the Society at least once in every month, except in the months of July, August, and September, or oftener should they see occasion; and three shall be a quorum, except in cases relating to the publication of Papers, when seven members must be present. A week's notice of each ordinary meeting shall be sent to every Member of the Council. Special Meetings of the Council may be summoned by the President, or by any three Members.

Quorum of  
Council.

Special  
Meetings of  
Council.

3.—The following questions, when brought before the Council, shall be determined by ballot:—The election of officers and Members of Council. The appointment of Referees. The acceptance of Papers. All other questions in the Council shall be determined by vote, or by ballot if demanded; and in case of an equality of votes, the President shall have a second or casting vote; except in cases relating to the acceptance of a paper: when, if the votes be equal, the further consideration of the question shall be adjourned to the next Meeting of Council; and if on a second ballot there shall still be an equality of votes, it shall be determined in the negative.

4.—The Council shall be empowered to refuse the publication in the Transactions of any Paper which has been read before the Society, should circumstances come to their knowledge which were not known when the Paper was accepted for reading.

5.—The Council shall be empowered to appoint, at their first Meeting after the Annual General Meeting, thirty-six Fellows of the Society, as Referees, to report to them confidentially on the merits of Papers offered to the Society, especially as to their fitness for publication in the Transactions of the Society.

6.—The Council shall annually appoint a Library Committee and a House Committee. They shall have it in their power to appoint as many other Committees as they may think useful for promoting the objects of the Society, and to admit into such Committees any Fellows of the Society, whether Members of the Council or not. Such Committees shall act upon the instructions which they receive from time to time from the Council, to whom they shall report their proceedings; and the appointment of all, except Scientific Committees, shall last for no longer time than up to the day of the succeeding Annual Meeting.

7.—The Council shall exercise such other powers and authorities as are given to them by the Charter and

Questions to  
be determined  
by vote or  
ballot.

Publication of  
Papers.

Referees to  
report on  
Papers.

Library and  
House  
Committees.  
Appointment  
of other  
Committees.

General  
powers of the  
Council.

Bye-laws; and shall from time to time make such regulations and issue such orders, not inconsistent therewith, as shall appear to them conducive to the good government of the Society, and to the proper management of its concerns.

5

## CHAPTER XIII.

### *Of the Society's Transactions.*

Printing of Transactions.

1.—THE Transactions of the Society, under the designation of MEDICO-CHIRURGICAL TRANSACTIONS, shall be printed at such times and in such a manner as the Council shall direct. 10

Who are entitled to receive copies.

2.—Every Fellow of the Society paying an annual contribution of Three Guineas, whose annual contribution is not three months in arrear, shall be entitled to receive one copy of each issue of the Transactions which may be published subsequently to his being admitted a Fellow; and the Council shall be empowered to present, in the name of the Society, copies of the Transactions to such scientific bodies as they may think proper. 15

Presentation copies.

Non-resident Fellows may compound for Transactions.

3.—Every Non-resident Fellow of the Society, on payment of the sum of Eight Guineas, in addition to the usual admission fee, shall be entitled to receive one copy of every volume of the Society's Transactions which may be published subsequently to such payment, provided his annual contribution be not more than three months in arrear. 20 25

Reprints of papers presented to the authors.

4.—Authors of Communications may, on application to the Secretaries, be furnished, at the expense of the Society, with fifty copies of every paper presented by them, and printed in the Medico-Chirurgical Transactions: but such copies are not to be delivered to them, unless by a special order of the Council, till the volume, or part which contains the Paper, is ready for publication. 30

## CHAPTER XIV.

*Of Scientific Committees.*

- 1.—THE Council shall, from time to time, appoint Committees of Fellows of the Society for the purpose of investigating questions of importance in Medical Science, and shall have authority to grant such sums of money as they may deem necessary for the expenses of these investigations. The Reports of such Committees shall be presented to the Council to be dealt with as may seem most <sup>Appointment of Scientific Committees.</sup> <sup>Reports published.</sup> <sup>advisable.</sup>
- 2.—Such Committees shall be called “Scientific Committees.” They shall consist of not less than three Fellows. The Secretaries of the Society shall, as far as possible, arrange that one of them shall take part in the <sup>Constitution of Scientific Committees.</sup> work of such committees.
- 3.—The Scientific Committees shall continue to act until they have reported upon the subject referred to them, or been dissolved by the Council. <sup>Dissolution.</sup>
- 4.—Every Member who has acted on a Scientific Committee shall sign the final Report, or shall state, in writing, his reasons for declining to do so. The Report shall be first received and considered by the Council, specially summoned for that purpose, and shall afterwards, with their sanction, be presented at an Ordinary General Meeting of the Society. All Reports shall be placed in the Library at least one week before the day fixed for their presentation. <sup>Final Reports.</sup>
- 5.—The Council shall be informed by their Secretary of the retirement of any Member of a Scientific Committee, in which case the Council may, at their discretion, appoint another Fellow of the Society to fill the vacancy. <sup>Retirement of Members.</sup>
- 6.—The names of the Fellows forming a Scientific Committee shall be placed in the Library of the Society. <sup>Names of Members placed in Library.</sup>
- 7.—The Scientific Committees shall render to the

All money to be accounted for.

Council an account of all moneys received by them for the purposes of their investigations.

Power of Council to dissolve Committee.

8.—The Council shall have the power to dissolve a Scientific Committee whenever they may deem it expedient.

5

## CHAPTER XV.

### *Of the Library.*

Management of Library by the Council.

1.—THE Library shall be under the management and direction of the Council, and be open on such days and at such hours as the Council shall direct. The Council shall be empowered to designate such works as shall not be allowed to circulate. 10

Borrowing of books.

2.—Every Fellow paying the annual contribution of Three Guineas, or having compounded for the same, and every Resident Honorary Fellow, shall be allowed to borrow books from the Library, and to have eight volumes in his possession at the same time. Every Non-resident Fellow paying the annual contribution of One Guinea shall be allowed to borrow books from the Library, but shall not have more than one volume at a time. Pamphlets and periodical publications are not to be kept above one week, nor any other book above two weeks. 15 20

Number of volumes and time allowed.

Fines for detention of books beyond stipulated time.

3.—When a book is wanted which has been in the possession of a Fellow the stipulated time, the Secretary shall send a notice by the post to the person in whose possession it may be, requesting the return of it; and a fine of Sixpence per day shall be incurred for every day that it may be detained, after the third from the transmission of such notice; and from the issue of such notice, and until the return of such work or works and the discharge of all fines incurred through delay, no further issue of books shall be permitted to such Fellow. 25 30

Books ordered in for inspection.

4.—The books shall be ordered in for inspection at such times as the Council shall appoint, and a fine of Five



Shillings per volume shall be incurred for neglecting to send in books by the time required in the notice.

5.—A book shall lie on the Library table, in which Books recommended by the Council for purchase. Fellows may insert, for the consideration of the Council or Library Committee, the titles of works which they think should be added to the Library.

6.—Fellows who borrow books from the Library shall be answerable for the full value of any work that may be lost or injured while in their keeping. Responsibility of borrowers.

10 7.—The Council shall have it in their power to collect the fines in the way which they may think best. Collection of fines.

## CHAPTER XVI.

### *Of the Ordinary General Meetings.*

1.—THE ordinary general meetings of the Society shall be held on the second and fourth Tuesday in the month, from the fourth Tuesday in October to the second Tuesday in June (both inclusive), at half-past eight o'clock in the evening. Meetings appointed for the election of Fellows shall commence at twenty-five minutes past eight o'clock. On the fourth Tuesday in December the Society shall not meet, nor on the usual Tuesday if it shall fall in Easter week, in which case there shall be a meeting on the fourth Tuesday in June. Ordinary General Meetings.

2.—Each Fellow of the Society shall have the privilege of introducing a stranger at every ordinary meeting, on delivering his name to the President or person acting in his stead; and the name of every stranger, so introduced, shall be entered in the Visitors' book; but no stranger shall be introduced more than three times in the same session. Introduction of strangers. Visitors' book.

3.—The business of the Society, at the ordinary meetings, shall be to read letters, reports and other papers on Medicine, Surgery, or any of the branches of Science connected therewith, and to converse upon professional subjects. Business at Ordinary Meetings.

4.—At the ordinary general meetings of the Society, nothing relating to its laws or management shall be brought forward.

Quorum.

5.—At ordinary general meetings, five shall be a quorum; but ten shall be necessary for the election of 5 Fellows.

Additional Meetings.

6.—Additional ordinary general meetings may be held when the Council may think them necessary.

## CHAPTER XVII.

### *Of the Annual General, and Special General, Meetings.* 10

Annual General Meeting on March 1st.

1.—THE Annual General Meeting of the Society, for the election of the Officers and other Members of the Council, shall be held on the 1st of March unless that day shall happen to be Sunday, in which case it shall take place on the day following. 15

Special General Meetings.

2.—The President and Council may, at any time, call a Special General Meeting of the Society, when it seems to them necessary; giving at least one week's notice, by letter, to every Fellow of the Society resident in the United Kingdom, of the time of meeting, and the 20 business upon which it is summoned: and no business shall be entered upon at such meeting except that which has been so notified.

Bye-laws—  
new proposals  
suspended in  
the Library.

3.—All proposals to enact, alter, or repeal, Bye-laws, shall be suspended in the Society's Library, for the in- 25 spection of the Fellows, from the time of the issuing of the summons of the General Meeting, at which it is intended to submit such proposals, for confirmation by two thirds of the Fellows present, pursuant to the Charter.

Recommend-  
ing new Bye-  
laws, and  
repealing or  
altering old  
ones.

4.—Any three Fellows may recommend new Bye-laws, 30 or the repeal or alteration of old ones, to the Council. The recommendations, duly signed, must be sent in writing to one of the Secretaries. On such recommendations the Council shall deliberate at their next meeting; if the

decision shall not be satisfactory to the said three Fellows, the Council, if required by them, shall at the Annual General Meeting, or some Special General Meeting bring the same forward, with their decision thereupon, for the  
5 opinion of the Society at large.

5.—No resolution carried by way of original motion, or as an amendment, at the Annual General Meeting (except resolutions with respect to the election of the Council, and other prescribed matters, and the usual business  
10 of such meeting) or any other General Meeting, of which notice shall not have been given in the circular summoning such meeting, shall be binding on the Society or Council, until such resolution shall be confirmed by a Special General Meeting, to be convened within fifteen days  
15 of the Meeting at which such resolution shall have been carried, by notice from the Council, stating the object of such Meeting, and the resolution or resolutions to be proposed for confirmation, and such notice shall be sent to all the Fellows at least five days previous to such  
20 Meeting, and no question shall be discussed at such Meeting, of which notice shall not have been given in the summons.

## CHAPTER XVIII.

### *Of the Society's Property.*

25 1.—THE whole of the Society's property and effects, of what kind soever, shall be under the direction, manage-  
ment, and control of the Council; but the Council shall  
not sell or mortgage any of the Society's lands, tenements, or hereditaments or invested funds without the sanction  
30 of a Special General Meeting of the Society or of the Annual General Meeting, due notice having been given of the business to be then taken into consideration.

2.—In order that this Society may in all respects con-  
form with the provisions of the Statute 6 and 7 Vic., chap.  
35 36, sec. 1, the funds of the Society shall at all times be

Confirming  
resolutions or  
amendments  
carried at  
General  
Meetings.

Management  
of the  
Society's  
property and  
effects.

All funds to  
be devoted to  
the purposes  
of the  
Society.

devoted to the purposes for which it was instituted, and no dividend, gift, division, or bonus in money, shall at any time be made unto or between any of the Fellows.

## CHAPTER XIX.

### *Of Donations to the Society.*

5

Donors' names to be entered on the minutes, and

1.—THE name of every person who shall present books, money, or any other property, to the Society, shall be entered on the minutes, with the mention of the gift; it shall be announced at an ordinary meeting, or the Annual General Meeting of the Society. 10

inserted in books presented.

2.—Books presented to the Society shall have the Donor's name inserted in them.

## CHAPTER XX.

### *Of the Common Seal and Deeds.*

15

The Common Seal of the Society.

1.—THE Common Seal of the Society shall be a representation of Salus raising a kneeling figure;\* with the motto, NON EST VIVERE, SED VALERE, VITA; † and the date of the formation of the Society, 1805; surrounded by a Garter, having on it, SIG. SOC. REG. MED. CHIR. LOND. 20

Custody of the Charter, Seal, and Deeds.

2.—The Charter, the Common Seal, and the Deeds of the Society shall be kept in safe custody in such manner as the Council shall from time to time direct.

Use of Common Seal.

3.—The Common Seal shall not be affixed to any deed or writing, except at a meeting of the Council, and by their authority. 25

\* Figura Muliebris stans; dextra, figuram virilem procumbentem sublevat; sinistra, baculum, serpente involutum, gerit.—From a rare medal of Caracalla, in the British Museum, described in Vaillant's Numismata Imperatorum Romanorum. 30

An engraving of the Society's Seal is given on the title-page.

† Martial, Epigram. Lib. 6, Ep. 70.

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